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A HOSPITAL BASED STUDY ON RETINOPATHY OF PREMATURITY: INCIDENCE AND RISK FACTORS IN PRETERM BIRTHS

Saumya Agrawal[1], Shashi Jain[2]
[1] - *Senior Resident, Dept. of Ophthalmology, SSMC, Rewa*
[2] - *Professor and Head, Dept. of Ophthalmology, SSMC, Rewa*

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Corresponding Author
Dr. Shashi Jain
Professor and Head,
Dept. of Ophthalmology,
SSMC, Rewa

Abstract:

Introduction: ROP is a vasoproliferative retinopathy of eye 1 which affects premature newborns which may progress and cause visual impairment. Though the disease is well known now, the magnitude of problem and various risk factors associated with or leading to it are yet to be established.

Objectives: To determine the incidence of ROP in Preterm babies in NICU (Neonatal Intensive Care Unit) of SSMC, Rewa and to study the risk factors associated with or leading to the disease and to correlate them with disease severity.

Material And Methods: Hospital based, retrospecttive study was carried out in NICU of SSMC which included all babies born before 34 weeks gestation and/or weighing < 1750 grams and babies born after 34-36 weeks and/or weighing 1750-2000 grams were included if they had risk factors of ROP.

Results: A total of 63 BABIES were initially included, of these three babies died and nine did not return for complete follow up. The remaining 51 preterm babies were examined as per protocol and 9 patients had ROP.

Discussion: According to our study, besides low birth weight and early gestational age, oxygen administration, apneic spells in infants, exchange transfusions given are significant risk factors for ROP. The sample size is small. To know the true incidence and risk factors involved it is advisable to undertake larger study over a period of years.

Conclusions: In developing countries, the incidence of ROP continues to rise with improvement in survival of extremely preterm infants. In developed countries, ROP is significantly reduced. Further research is required to fully understand and prevent ROP. Appropriate screening and treatment strategies will be needed in reducing blindness in developing countries.

Keywords: Retinopathy of Prematurity, Risk factors, preterm births

Introduction

ROP is a vasoproliferative retinopathy of eye[1] which affects premature newborns which may progress and cause visual impairment. Two ROP epidemics occurred in industrial developed countries during the past 60 years. According to Campbell, ROP occurred with oxygen supplementation to premature children. But later it was found that oxygen is not the sole cause of this potentially blinding disease. There are several risk factors which include LBW, Low Gestational age,

exposure to oxygen,septicaemia and blood transfusion, dopamine use, multiple birth, chronic lung disease, RDS, HMD, seizure disorder, phototherapy, icterus, anaemia, low APGAR Score, cyanosis, sepsis[2] etc. As the health care is improving these days, so is the number of preterm infants and consequently ROP. All births before 31 weeks of gestation or weighing <= 1500 grams should be screened in 3-4 weeks. Children weighing less than this or born before this should be screened even early. Though the disease is well known now, the magnitude of problem and various risk factors associated with or leading to it are yet to be established.

Objectives

To determine the incidence of ROP in Preterm babies in NICU (Neonatal Intensive Care Unit) of SSMC, Rewa. Also, to study the risk factors associated with or leading to the disease and to correlate them with disease severity.

Material And Methods

A hospital based, retrospecttive study was carried out in the Department of Ophthalmology of SSMC, Rewaand Neonatal Intensive Care unit (NICU) of the same hospital

Inclusion criteria

All babies born before 34 weeks gestation and/or weighing < 1750 grams were included. Babies born after 34-36 weeks and/or weighing 1750-2000 grams were included if they had risk factors of ROP.[3]

Exclusion criteria

1. Babies who died before examination or before full retina is vascularised.
2. Loss to follow up due to other reasons.
3. Babies with other ocular disorders, which interfere with fundus examination and those with other congenital retinal abnormalities.
4. Those who did not give consent were excluded from the study.

When to screen all eligible babies at

1. 31 weeks PCA (post conceptional age) or 3-4 weeks after birth (whichever earlier)
2. No examination needed in first 3 weeks of life
3. Next date of examination to be decided by the ophthalmologist based on initial findings
4. One complete screening session should be definitely carried out before ‘Day 30’ of life of infant[4].

The 20-30 Day strategy is most effective in preventing ROP blindness and needs to be strictly adhered to by all. Delaying the timing of first screening increases the likelihood of seeing advanced disease, especially in the APROP eyes, with consequent reduced success rates.

Eye drop used in our study is tropicamide 1% with phenylephrine 2.5%. Drops to be repeated after every five minutes. Pupils usually dilate in 20-30 minutes and remains dilated for 45 minutes to one hour.

The place of screening should be hygienic enough for the neonate. It is to be noted that in severe plus disease, pupillary dilation is impaired. In case of doubt, do not continue dilating eye drops beyond a limit as this can cause systemic toxicity.

A condensing lens of 20D was used for this purpose. Only 20 D lenses were advocated to judge plus disease, defined as dilatation and tortuosity of at least two retinal vessels. Plus also includes retinal hemorrhages, NVI and vitreous haze. Disc, macula and retinal vessels were evaluated for plus disease, vessel loops or avascular retina. In zone II examination of peripheral retina nasally till ora. Avascularity here would denote disease in zone II. And avascular area only in the temporal retina would qualify the disease for zone III. The zones and stages of the disease (Stage I-V), with or without Plus component are specified.

Statistical Methods

Results on continuous measurements were presented on Mean ±SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Chi-square/Fisher Exact test was been used to find the significance of study parameters on categorical scale between two or more groups.

Risk Factors For ROP

Birth weight and gestational age

The incidence and severity of ROP is inversely related to birth weight and gestational age[5]. Infants with very low birth weight (<1000g) are particularly at risk.

Oxygen therapy

Oxygen has toxic effect on immature vessels[6]. Though several controlled trials (Patz et al 1952; Lanman et al 1954; Kinsley et al 1956) compared high and low supplemental oxygen in premature infants confirmed the relationship between oxygen therapy and ROP, it has not been possible to define safe level of oxygen usage for clinical practice.

Blood transfusion and ROP It has been identified as a risk factor for ROP in several studies[7], some investigators, however, could not confirm this association. This could be explained by the fact that tissue (and thereby retinal) oxygen levels are increased by transfusions due to the reduced oxygen affinity of adult as compared to fetal hemoglobin.

Anemia

The presence of significant anemia is usually associated with administration of blood transfusion. Thus in patients who are anemic and have been given blood transfusion and have developed ROP, it is difficult to pin point anemia or blood transfusion as the possible cause.

Multiple gestations

Frilling et al (1997) studied occurrence of ROP in multiple gestations, very low birth weight. He showed that in twins the second born baby was at a higher risk for ROP but, it was mainly due to low birth weight and that birth weight was a more significant indicator of ROP than birth order.

Light exposure

A relationship between light exposure and retinopathy of prematurity was first suggested by Terry in his original descriptions

Apnoea and ventilation

Apnoea was found to be a significant risk factor for ROP in many studies like Hammer et al (1996). SwarnaRekha et al(1996) has found apnoea to be a risk factor for development of ROP.

Sepsis:

Sepsis is also a postulated risk factor for development of ROP. Sepsis may act through cytokines and endotoxins or by oxidative burst in the neutrophil consequent to infection. Maheshwari et al(1996) found sepsis to an independent risk factor for ROP.

O_2 free radicals are one of the causes of injury to the developing retinal capillaries in the preterm infants. Energy from light striking the retina may induce/increase the number of O_2 free radicals in the retina particularly in phase of high levels of tissue O_2.

Maternal risk factors

Certain pathologic conditions in the mother have been postulated to be related to the development of ROP in newborn. The factors which are likely to be involved and need careful analysis for association are:-

- Maternal bleeding
- Leaking per vaginum (LPV)
- Abruption placentae
- Placenta praevia
- Diabetes
- Pre-eclamptic toxemia

Treatment

Threshold ROP is treated with in 72hrs by ablation of the vascular retina by laser or cryotherapy. Laser is superior in view of ease of delivery, no general anesthesia required, more effective in zone 1, i.e. in treating the posterior pole and less induced myopia.

Results

A total of 63 babies initially satisfied the inclusion criteria, of these three babies died and nine did not return for complete follow up. They were excluded from the study. The remaining 51 preterm babies were examined as per protocol and 9 patients had ROP.

Table 1. Incidence of ROP

Stage	No. Of Babies	Percentage
0	42	82.35
I	2	3.92
II	4	7.8
III	1	1.96
IV	1	1.96
APROP	1	1.96

Table 2- Incidence of ROP in different ranges of birth weight.

Birth wt in gms	Total patients	ROP patients	Incidence of ROP
750-1000	2	2	100%
1001-1250	6	3	50%
1251-1500	12	2	17%
1501-1750	15	1	7%
1751 onwards	16	1	6%

Table 3:- Incidence of ROP in different ranges of gestational age

Gestational age in weeks	Total patients	ROP Patients	Incidence of ROP
≤28	4	3	75%
29	4	1	25%
30	3	1	33%
31	4	1	25%
32	13	2	15.38%
33	7	1	14.28%
34	4	0	0
35	6	0	0
36	6	0	0

Table 4:- Association of ROP with septicaemia (SEP)

	SEP -nt	SEP +nt	Total	P Value	Significance
ROP –nt	32	9	41	0.037	S
ROP +nt	4	5	9		
Total	36	15	51		

Table 5:- Association of ROP with phototherapy (PhT).

	Pht -nt	PhT +nt	Total	P Value	Significance
ROP absent	30	12	42	0.12	NS
ROP present	4	5	9		
Total	34	17	51		

Table 6:-Association of ROP with apnoeic spells (APN).

	APN -nt	APN +nt	Total	P Value	Significance
ROP absent	38	4	42	0.009	S
ROP present	5	4	9		
Total	43	8	51		

Table 7:- Association of ROP and oxygen administration

	O2 -nt	O2 +nt	Total	P Value	Significance
ROP absent	25	17	42	0.042	S
ROP present	2	7	9		
Total	27	24	51		

Table 8:- Association of ROP with respiratory distress

	Resp -nt	Resp +nt	Total	P Value	Significance
ROP absent	27	15	42	0.27	NS
ROP present	4	5	9		
Total	31	20	51		

Table 9:- Association of ROP with exchange transfusion (ET)

	ET -nt	ET +nt	Total	P Value	Significance
ROP absent	39	8	47	0.028	S*
ROP present	7	6	13		
Total	46	14	60		

Discussion

According to our study, besides low birth weight and early gestational age, oxygen administration, apneic spells in infants, exchange transfusions given to them, and septicemia have significant impact on development of ROP. The actual incidence of ROP may vary from place to place and time to time, even in the same nursery. Studies from India have given incidences as varied as 20% (Maheshwari et al 1986), 22%

(Kumar et al, 1995), 38% (Gopal et al, 1995), 46% (Swarnarekha et al, 1996) and 47.76% (Charan et al, 1994)[8]. The incidence of detection in our study was 17.65%. This correlates well with the studies of Kumar et al and Maheshwari et al[9].

The incidence of ROP in our study correlates well with the studies of some foreign authors; 21.5% (Darrow et al, 1992)113, and 21.3% (Hussein et al, 1999)114. The inclusion criteria was birth weight <1500 gm and gestational age at birth<36 weeks, respectively was quite similar to ours. The reported incidence in similar birth weight (<1500 gm) babies in other recent studies was 27.4% (Schalij Delfor et al, 1996)115, 35% and 50.9% (Fielder et al 1992)116. Their population of babies <1000 gm birth weight was 34.4% and 12.5% respectively compared to ours of 1.7%. This could account for higher incidence of ROP in their studies.

Our study has few limitations. The sample size is small. To know the true incidence and risk factors involved it is advisable to undertake larger study over a period of years. It is quite possible that risk factors such as maternal infections, maternal history of infertility treatment and genetic mutations in these infants responsible for diseases mimicking ROP, not evaluated in this study may have influenced the results.

Our manpower, efforts and funds should be directed towards the 23.1% babies with ROP who are at risk for blindness. Since each nursery is likely to have a variable population at risk, it is our proposal that each nursery must have a screening program to identify the same as applicable to their nursery. This would ensure that preterm babies actually at risk for blindness due to ROP get timely and decisive intervention.

Conclusions

In developed countries, the incidence of ROP continues to rise with improvement in survival of extremely preterm infants. The present study underlines the magnitude of the problem due to ROP in a tertiary care centre.

1) Temporal quadrant was involved most frequently purely nasal involvement was never seen.

2) We found postnatal age to be more reliable than post conceptional age and ROP onset correlated better with postnatal age than post conceptional age.

3) Plus disease (retinal vascular dilation and tortuosity) was found to be a reliable predictor of the disease, resistance of the pupil to dilatation should alert the ophthalmologist to the possible presence of the disease.

4) ROP was found to occur significantly more frequently at lower mean birth weight while it was significantly more severe at lower birth weight.

5) ROP was found to occur significantly more frequently with lower gestational age but there was no significant influence of gestational age on the severity of ROP.

6) In our opinion, the effective management of retinopathy of prematurity requires a team effort of the neonatologist, ophthalmologist and NICU staff. Thus every nursery should have a screening program and establish its own inclusion criteria.

In developed countries, ROP is significantly reduced. Further research is required to fully understand and prevent ROP. Appropriate screening and treatment strategies will be needed in reducing blindness in developing countries.

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