INCIDENCE OF RETINOPATHY OF PREMATURITY AND RISK FACTORS IN VERY LOW BIRTH WEIGHT INFANTS IN A NEONATAL INTENSIVE CARE UNIT IN A UNIVERSITY HOSPITAL IN BRAZIL

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Background and aims:

Retinopathy of prematurity (ROP) occurs when abnormal blood vessels grow and spread throughout the retina in immature retina. The disease is one of the main causes of childhood blindness in the world. Risk factors include low birth weight (VLBW), prolonged oxygen therapy, blood transfusions, use of surfactant, septicemia^{1,2,3,4}. The aim of this study was to evaluate the incidence of ROP, associated risk factors, in neonates with birth weight ≤1,500 grams and / or gestational age ≤32 weeks (VLBW) in a neonatal intensive care unit (NICU) at the University Hospital in Canoas.

Methods

Retrospective study of infants admitted in NICU during two years (2015-2016). Inclusion criteria was all the VLBW discharged from NICU in the study period. The eye examination was carried out on the 28th day of life. In cases where ROP was diagnosed, they were followed weekly, by the same pediatric ophthalmologist . The analysis technique included pupil dilation with phenylephrine 2.5% + tropicamide 0.5%, one hour before examination. it was used anesthetic eyedrops of proximetacaine and carried out retinal mapping in 360 ° with lens of 28 diopters, by means of indirect ophthalmoscopy. Quantitative variables were described by mean and standard deviation or interquartile range and median. Qualitative variables were described by absolute and relative frequencies. To compare means, the t-student test was applied. In asymmetry, the Mann-Whitney test was used. In the comparison of proportions, Pearson's chi-square or Fisher's exact tests were applied. For control of confounding factors, the Poisson Regression analysis was applied. To determine the best cutoff point for ROP, considering the time of mechanical ventilation and gestational age, the Receiver Operating Characteristic curve (ROC) was applied prioritizing the sensitivity of these variables. The level of significance was 5%. The SPSS software version 21.0 was used. The study was approved by the research ethics committee of the Lutheran University of Brazil, under protocol number 2008-546H.

Results

Were included 92 patients, and the incidence of ROP was 14.1%. The risk factors associated were gestational age (p = 0.001), birth weight (p = 0.032), surfactant use (p = 0.030), mechanical ventilation (p = 0.013), mechanical ventilation time (p = 0.003), corrected gestational age at discharge (p = 0.002) and length of hospital stay (p <0.001). The variables studied can be seen in Table 1. The factor with better prediction was hospitalization time, increased risk in 5% for each day of hospitalization. The incidence of ROP in this study was similar found in the literature in developed countries⁵. Supplemental oxygen use is associated with ROP, but it is not yet known exactly how much oxygen saturation should be maintained in premature infants. Several studies have shown that decreased saturation leads to lower ROP rates⁶, but with an increase in mortality. The University Hospital of Canoas maintains saturation between 90% and 95% as a target⁷. In this study, the use of mechanical ventilation (MV), oxygen supply and the duration of the MV showed statistical significance. With 11 days of MV, the sensitivity for the risk of developing ROP among the patients evaluated is 100% (table 2).

After adjusting for the multivariate model, only gestational age and length of hospital stay remained statistically significant. For a one-week increase in gestational age, there is a 24% reduction in the incidence of retinopathy (RR=0.76; 95% CI: 0.63 - 0.92 p>0.004) and for a one-day hospitalization, there is an increase in the incidence of ROP in 5% (RR=1,05; 95% CI: 1.03 - 1.06 p <0.001).

Variables	ROP (n=13)	No ROP (n=79)	p
Maternal Data			
Pre-eclampsia – n (%)	7 (53,8)	27 (34,2)	0,219
Maternal steroids – n (%)	11 (84,6)	59 (74,7)	0,726
Magnesium Sulfate – n (%)	5 (38,5)	33 (41,8)	1,000
Maternal drugs – n (%)	0 (0,0)	4 (5,1)	1,000
Newborn Data			
GA – mean ± SD	28,8 ± 1,8	30,4 ± 1,4	0,001
Nutritional Status – n (%)			0,927
SGA	5 (38,5)	35 (44,3)	
AGA	8 (61,5)	44 (55,7)	
Weight – mean ± SD	1034 ± 294	1183 ± 216	0,032
Male – n (%)	5 (38,5)	42 (53,2)	0,494
APGAR 5' – md (p25-p75)	9 (8-9)	8 (7-9)	0,218
Surfactant – n (%)	12 (92,3)	48 (60,8)	0,030
Hyperglycemia – n (%)	1 (7,7)	7 (8,9)	1,000
MV – n (%)	11 (84,6)	34 (43,0)	0,013
MV Duration – md (p25 – p75)	40 (15-61)	14 (3-25)	0,003
Nasal CPAP – n (%)	11 (84,6)	72 (91,1)	0,610
CPAP duration – md (p25 – p75)	8 (6-19)	5 (3-13)	0,073
Oxygen duration – md (p25 – p75)	17 (9-27)	7 (3-17)	0,073
Sepsis – n (%)	13 (100)	63 (79,7)	0,114
Early onset sepsis – n (%)	12 (92,3)	49 (62,0)	0,054
Late onset sepsis – n (%)	11 (84,6)	42 (53,2)	0,068
NEC – n (%)	1 (7,7)	13 (16,5)	0,683
Blood transfusion – n (%)	10 (76,9)	36 (45,6)	0,073
Apnea – n (%)	10 (76,9)	64 (81,0)	0,714
Jaundice – n (%)	7 (53,8)	58 (73,4)	0,191
Weight at discharge – average ± SD	2.387 ± 414	2.089 ± 237	0,075
GA corrected at discharge – mean ± SD	41,0 ± 3,3	37,5 ± 2,2	0,002
Hospital stay – mean ± SD	85,3 ± 23,7	51,7 ± 19,2	<0,001

Table 1. Risk factor for ROP in the VLBW group
MV = Mechanical ventilation; md = median; SD = standard deviation; P25 = percentile 25; P75 = percentile 75; SGA = small for gestational age; AGA = adequate for gestational age; CPAP = continuous positive airway pressure; NEC = Necrotizing enterocolitis; ROP = retinopathy of prematurity; GA = Gestational age

Variables	Cutoff	Sensibility	Specificity	AUC	CI 95%	p
MV duration	≥11 days	100%	50%	0,79	0,60-0,98	0,025
Hospital stay	≥56 days	84,6%	67,1%	0,85	0,74-0,97	<0,001
Gestational age	<30 weeks	69,6%	69,2%	0,77	0,63-0,91	0,002
Birth weight	<1125g	70,9%	69,2%	0,68	0,50-0,86	0,038

Table 2. ROC curve analysis to determine the best cutoff points of the time of mechanical ventilation and gestational age for ROP
AUC = area under the curve; CI = confidence interval; MV = Mechanical ventilation.

Conclusion

The incidence of ROP in VLBW was 14.1%. The risk factors were gestational age at birth, mechanical ventilation duration and the length of hospital stay.

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