CORRELATIONS BETWEEN OXYGEN THERAPY AND RETINOPATHY OF PREMATURITY (ROP) - STUDY OF A GROUP OF 11 PREMATURE INFANTS WITH ROP REQUIRING TREATMENT

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Abstract

Retinopathy of prematurity (ROP) is the most common ocular abnormality in premature infants. It is a neovascular disorder and its incidence increases with decreasing gestational age and decreasing birth weight. It has a multifactorial etiology, primarily due to immaturity and avascular retina.

Aim of the study: The aim of this study is to establish correlations between the forms of ROP requiring treatment as a complication of prematurity and the associated therapeutic or pathogenic factors. Regarding the used therapeutic factors we have insisted on oxygen therapy.

Material and method: 293 premature infants with gestational age less than 34 weeks, born in Maternity Hospital in Oradea in the period 01st of January 2011 – 31st of December 2013 were included in this study. All these premature infants were evaluated by an ophthalmologist at 1 month postnatal age or at 34 weeks corrected age for early detection of retinopathy of prematurity. Our study focuses on a group of 11 premature infants who experienced retinopathy of prematurity, stage 3, and required surgical correction.

Conclusions: Several risk factors have been reported as predisposing to the development of ROP: oxygen therapy, anemia, red blood cell transfusion, sepsis, and apnea. In our study proved to be significant risk factors: oxygen therapy, sepsis, congenital pneumonia and especially repeated apnea requiring treatment (81,81% in the group of infants with ROP vs. 40% in the group of infants without ROP). The variations in hemoglobin oxygen saturation, variations occurring during and after apnea, are involved in the onset and evolution of retinopathy of prematurity. The exposure to alternating hypoxia and hyperoxia increases the incidence of retinopathy and causes severe proliferative retinopathy, requiring treatment.

Key words: premature, oxygen therapy, retinopathy of prematurity

Introduction

The premature infants may show multiple abnormalities of different visual system components.[1,2,3]

ROP is the most common ocular abnormality in premature infants. It is a neovascular disorder and its incidence increases with decreasing gestational age and decreasing birth weight. It has a multifactorial etiology, primarily due to immaturity and avascular retina.[4] Other factors, including hypoxia, hyperoxia, variations in blood pressure, sepsis, acidosis, may injure the endothelium of the immature retinal blood vessels. The retina enters a passive phase and forms a pathognomonic structure of mesenchymal cells between the vascularized and the avascular regions of the retina by 33 to 34 weeks of postmenstrual age. In some infants, this structure regresses and it remains only the vascularized retina. In other infants, abnormal blood vessels proliferate from this structure and the progressive disease can cause exudation, hemorrhage and fibrosis, with subsequent scarring or retinal detachment. The presence of plus factor, with dilated and tortuous blood vessels in the posterior pole of the eye may be associated with an adverse visual outcome.

The international classification of ROP: *Committee for the Classification of Retinopathy of Prematurity (Aug 1984). "An International Classification of Retinopathy of Prematurity". Arch Ophthalmol. 102 (8): 1130–1134. doi: 10.1001/archopht. 1984.01040030908011. PMID 6547831.*

- Stage 1: presence of a white limiting line
- Stage 2: presence of a ridge
- Stage 3: presence of an extraretinal vascular tissue
- Stage 4: Partial retinal detachment
- Stage 5: Total retinal detachment (Figure 1)

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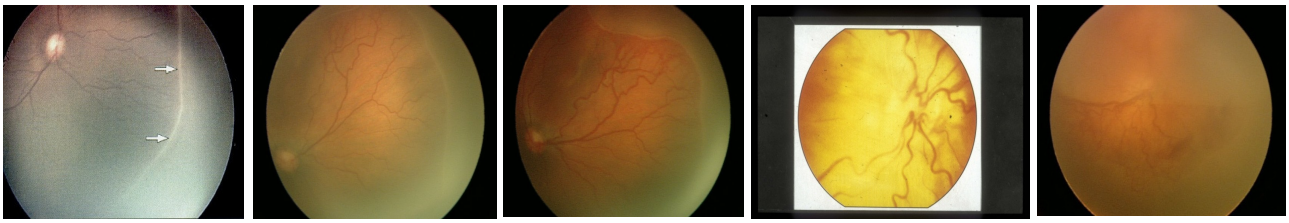


Figure 1: Retinopathy of prematurity, different stages.

There is much interest in the role of oxygen in retinopathy of prematurity. The optimal blood oxygen levels and hemoglobin oxygen saturation levels remain controversial.[5,6,7] Excessive oxygen in the first few weeks of postnatal life represents a major risk factor for retinopathy of prematurity.[8,9,10] Many studies have used protocols involving low oxygen saturation in order to decrease the incidence of ROP. The results were not statistically significant.[11,12,13,14,15,16] The results of other studies have suggested that increased hemoglobin oxygen saturation at higher gestational age decreases the risk of progression of ROP.[16,17] The study STOP-ROP tried to demonstrate that from a certain critical evolutionary threshold of ROP, the hyperoxia has a beneficial effect.[16] Theoretically this assumption makes sense because there is a suppression of the vascular endothelial growth factor and therefore of the vascular proliferation. It was noticed that in the hyperoxia group (hemoglobin oxygen saturation = 96-99%) the eye damage was reduced, but there were more pulmonary complications and it was significantly higher the need for oxygen therapy and hospitalization. It is interesting the fact that the infants with hemoglobin oxygen saturation above 94%, under atmospheric air condition und that weren't included in the study showed a favorable evolution in comparison to the infants that were included in the study and had hemoglobin oxygen saturation above 94% under higher FiO2 conditions.[15] This observation presents that the infants with spontaneous increased saturations have a protection against the side effects of hyperoxia.

Aim of the study

The aim of this study is to establish correlations between the forms of ROP requiring treatment as a complication of prematurity and the associated therapeutic or pathogenic factors. Regarding the used therapeutic factors we have insisted on oxygen therapy.

Material and method

A number of 293 premature infants with gestational age less than 34 weeks, born in Maternity Hospital in Oradea in the period 01st of January 2011 – 31st of December 2013 were included in this study. All these premature infants were evaluated by an ophthalmologist at 1 month postnatal age or at 34 weeks corrected age for early detection of retinopathy of prematurity. Our study focuses on a group of 11 premature infants who experienced retinopathy of prematurity, stage 3, and required surgical correction.

We obtained data from the observation sheets and monitoring sheets of the infants from the two groups: the first group consists of 11 premature infants with ROP, stage 3 and the second group consists of 15 premature infants without retinal damage and that presented similar clinical and demographic criteria:

We compared the two studied groups:

- associated pathology – the presence of idiopathic respiratory distress syndrome, maternal and fetal infection, congenital pneumonia, cerebral hemorrhage;
- complications: apnea in premature infant, bronchopulmonary dysplasia;
- established treatment: administration of surfactant, CPAP, assisted mechanical ventilation, free-flow oxygen therapy, blood transfusion;
- days of hospitalization.

Results and discussions

The total number of premature infants with gestational age < 34 weeks: 342 represents 2,73 % of the total number of infants.

Infants with gestational age < 34 weeks, evaluated for retinopathy: 293

Of 293 infants with gestational age under 34 weeks, 11 infants presented retinopathy of prematurity, stage 3, and required treatment.

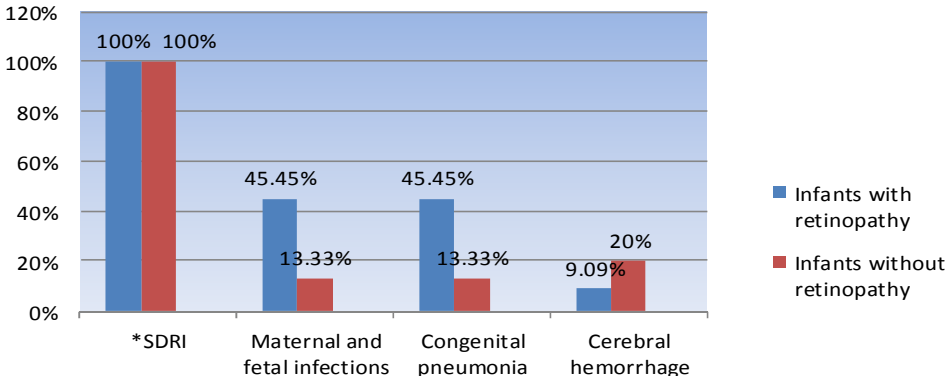
A number of 293 infants with gestational age under 34 weeks received screening for the detection of the retinopathy of prematurity. Of these newborns a number of 11 infants presented severe retinopathy requiring treatment. The incidence of severe retinopathy was of 3,75%, similarly to other published studies.[18,19]

These 11 infants represent the first studied group. The second group consists of 15 infants, selected after similar clinical and demographic criteria and that didn't present retinopathy of prematurity. (Table 1).

Table 1: Clinical and demographic criteria.

	Infants with ROP ST. III, IV- 11	Infants without retinal damage - 15
Average weight (grams)	1064,54	1102,24
Average gestational age (weeks)	28,45	28,15
Average Apgar score	2,72	2,9
Sex male	6	6
Sex female	5	5
Multiple pregnancy	3	1

Several risk factors have been reported as predisposing to the development of ROP: oxygen therapy, anemia, red blood cell transfusion, sepsis, apnea.[20,21,22,23,24] In our study proved to be significant risk factors: oxygen therapy, sepsis, congenital pneumonia and especially repeated apnea requiring treatment (81,81% in the group of infants with ROP vs. 40% in the group of infants without ROP) (Figure 2, 3, 4, 5).



* SDRI = idiopathic respiratory distress syndrome

Figure 2: Associated pathology in the studied premature infants from the two groups.

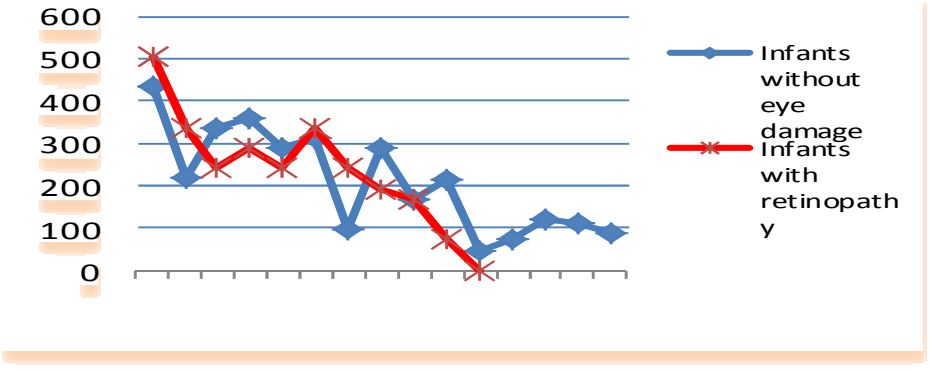


Figure 3: Number of hours of CPAP/ Average number of hours.

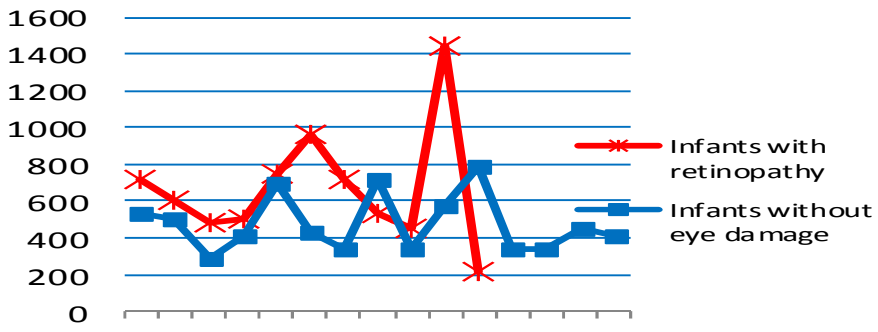


Figure 4: Total number of hours of oxygen therapy/ Average number.

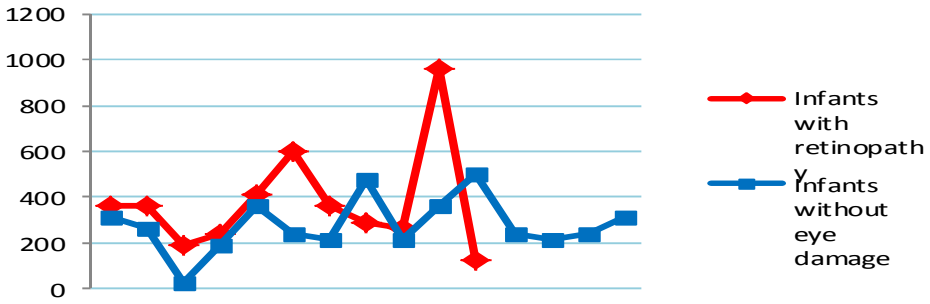


Figure 5: Oxygen therapy at FiO_2 under 40% / average number of hours.

The variations in hemoglobin oxygen saturation, variations occurring during and after apnea, are involved in the onset and evolution of retinopathy of prematurity (Figure 6). The exposure to alternating hypoxia and hyperoxia increases the incidence of retinopathy and causes severe proliferative retinopathy, requiring treatment. (Figure 7) These results correlate with many studies that present that the variations in oxygen saturation have adverse effects especially when hyperoxia is followed by hypoxia. It was demonstrated that the severe retinopathy is associated with a high variability of oxygen tension in the first 2 weeks of life.[25] The analysis of the risk factors for retinopathy help us to understand and to prevent its development and evolution.

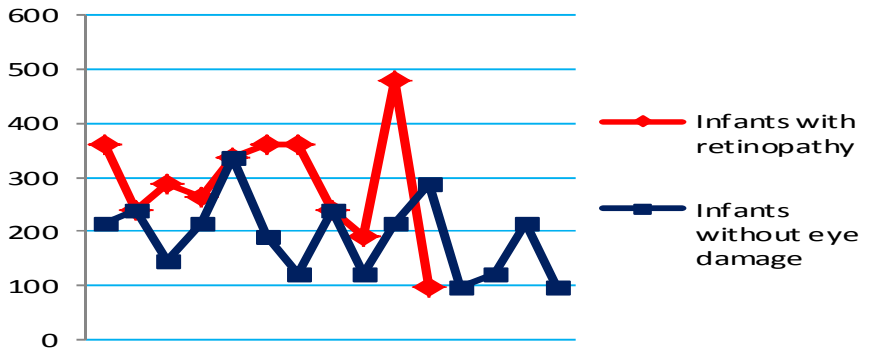


Figure 6: Oxygen therapy at FiO_2 above 40% / average number of hours.

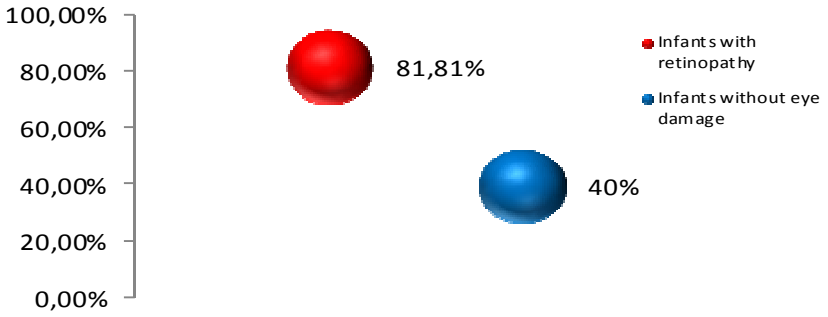


Figure 7: Repeated apnea requiring treatment with respiratory analeptics.

Conclusions

The simplest and safest method to decrease the incidence of retinopathy of prematurity is the strict control of the hemoglobin oxygen saturation.

This saturation should not exceed the values of 93% - 92% in extremely low birth weight infants.

Despite the enormous progress in recent years, there are still many open questions that will hopefully be elucidated in the near future.

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