Retinopathy of prematurity after Oxygen therapy, a prospective study in NICUs, Fayoum, Egypt

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ABSTRACT

Retinopathy of prematurity (ROP) is a vasoproliferative disease of an immature retina in premature neonates. It is the commonest cause of preventable blindness in infancy and childhood. ROP progresses in two phases. The first phase begins with delayed retinal vascular growth after birth and partial regression of existing vessels, followed by a second phase of hypoxia-induced pathological vessel growth. Two major risk factors of ROP are the use of Oxygen and a decreased gestation period. The relation between hyperoxia, low-gestational age, growth retardation, Oxygen dependent growth factors, and oxidative stress are now being understood more clearly. We know that in the first phase of retinopathy of prematurity, hyperoxia inhibits vascular endothelial growth factor. In the second phase, vascular endothelial growth factor rises, and when insulin-like growth factor-1 reaches a threshold around 32 to 34 weeks post-conceptional age, uncontrolled neo-vascularization may occur.

KEYWORDS: Retinopathy, prematurity, hypoxia, gestational age, IGF-1

INTRODUCTION

In the treatment of premature neonates, Oxygen therapy was first used and suggested by Tarnier in 1899, and continuous Oxygen therapy that lasting for several weeks as a routine treatment of premature neonates was introduced in Boston in 1930.**[1]** First case of ROP was discovered in 1942. It was not aggressive Oxygen therapy, but may be introduction of tighter new incubators which allowed Oxygen saturation to be maintained at a higher level.**[2]**

Retinopathy of prematurity (ROP) is a major cause of blindness in children in the developing and developed countries. Formerly known as retrolental fibroplasia, and was first described in the 1940s by Terry who first connected the disease with the premature neonates.**[3]**

The exact balance between high Oxygen supplementation to prevent death in early postnatal period and lower Oxygen supplementation to prevent vessel loss in ROP remains unsettled, and remains important issue in neonatology.**[4]**

IN spite of its vital role in life, Oxygen is also potentially toxic, as it can react with

prooxidants and produce Oxygen reactive species that cause inflammation and even cell death later on. Incomplete vascularized retina is highly susceptible to Oxygen. Thus, the more immature retinal vascularization, the greater affection by Oxygen toxicity.**[5]**

Premature infants are more susceptible to Oxygen toxicity due to low levels of antioxidant vitamins A, E, and C and antioxidant enzymes. Hypoxia and Hyperoxia have been implicated in retinal injury in premature neonates. Preterm birth results in exposure of the preterm neonates to a higher Oxygen concentration extra uterine, opposing to in-uterine. This relative hyperoxia postnatal results in slowing, cessation, and even regression of development of retinal vasculature. With time, the retina grows in thickness without sufficient blood vessel growth. Hypoxia occurs at level of the tissue, resulting in increased the release of angiogenic growth factors (e.g., VEGF) resulting in ROP.**[6]**

The optimum Oxygen saturation in different gestational ages and optimum saturation in each phase of ROP still unknown, although hyperoxia can have different effects during phase 1 than it does in phase 2 (when vascular proliferation is taking place).

Theoretically, several studies have examined that Oxygen in phase 2 of ROP could decrease high concentrations of Oxygen-regulated growth factors such as VEGF which cause proliferative disease.**[7]**

IN spite of no study reported the best SpO_2 target saturation, targets saturation should be differing in different phases and stages of ROP. Minimizing alternation of hypoxia and hyperoxia and prevent of undesired high Oxygen saturations in phase 1 of ROP seem to be the most important and promising techniques to prevent ROP.**[8]**

Methods

A prospective multi-center study was conducted on 212 preterm infants (GA<37 weeks) admitted in neonatal intensive care units at Fayoum university hospital or referred from nearby hospitals for ROP screening. They were subjected to history taking and clinical examination, possible risk factors such as

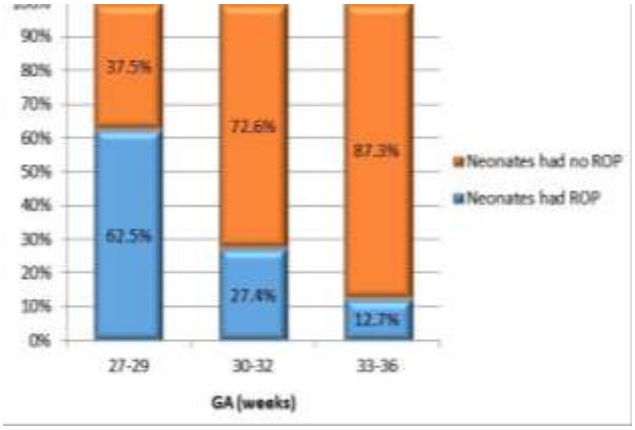

Figure1: *correlation between ROP and gestational age.*

multiple birth, GA, BW, sex, mode of delivery, Oxygen therapy, surfactant therapy, mechanical ventilation.

Pupils of both eyes were dilated with combined Cyclopentolate (100 mg/ml) and Phenylephrine (10 mg/ml) drops half an hour before examination (one drop, 5–10 min apart). After pupillary dilatation, ophthalmological examination was performed using a sterile pediatric eye speculum (Barraquer wire speculum 9 mm blade; S1-500-00, PK], following instillation of Benoxinate Hydrochloride 0.4% eye drops for topical anesthesia. Fundus examination was performed using indirect ophthalmoscope with 28D lens and scleral depression. The ROP status of each infant was classified according to the International Classification of ROP, including

stage, zone, and presence or absence of plus disease.

Results:

A total of 212 preterm neonates were screened for ROP who were admitted to Neonatal intensive care unit in Fayoum university hospital or referred from nearby hospitals in Fayoum government. Female sex represented 51.4%. The mean GA was 32±1.4 weeks (range: 27–36 weeks). The mean BW was 1600±302 g (range: 800-2000 g). 197 neonates were appropriate for gestational age (AGA), while one neonate was large for gestational age (LGA) and 14 neonates were small for gestational age (SGA).

In O_2 supplementation as a treatment, both concentration of O_2 and duration of exposure showed a statistically significant increase in ROP group.

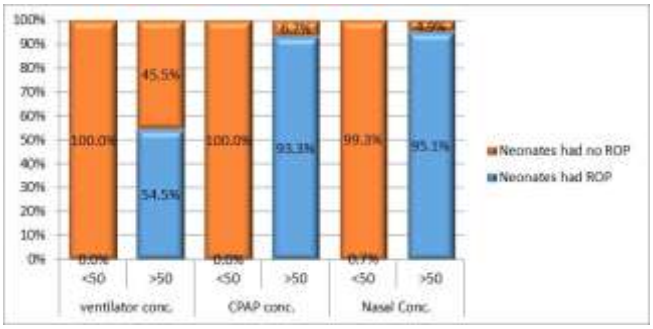

Figure2: *correlation between ROP and O2 therapy.*

DISCUSSION

Retinopathy of prematurity (ROP), a disease of immature retina in premature neonates, it is most common cause of blindness in infancy. [9]

In case of lack of early diagnosis and treatment, ROP can cause visual impairment up to blindness. It is now considered the commonest cause of preventable blindness in children.**[10]**

The present study revealed an incidence of ROP of 18.9 %. The incidence of the disease has varied in different previous studies from 11 to 60 %.

Our study revealed that exposure to O_2 for long durations and with high concentration increased significantly the incidence of ROP. ***Bassiouny et al*** in 2017 documented a strong association between Oxygen delivery and ROP although there was no data available about the duration and concentration of Oxygen. On the other hand, some studies proved no significant relationship between Oxygen and occurrence of ROP ***(Karkhaneh R et al., 2008).*****[11-12]**

Some authors revealed that the duration of Oxygen therapy was directly proportional to ROP development. In addition, the fluctuation in Oxygen exposure resulting in hyperoxia (>3 episodes) and hypoxia (2–3 episodes) was known to be a significant risk factor of the disease ***(Singh PH., 2016)***.**[13]**

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CONCLUSION

In our study, we investigated risk factors related to the development of ROP, These risk factors included low GA and BW, nasal continuous positive airway pressure (CPAP), intermittent mechanical ventilation, We found that these factors were significantly related to the occurrence of ROP and development of the severe form of the disease.

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