



Incidence of Retinopathy of Prematurity in Preterms on Vitamin A Supplementation in NICU of Tertiary Care Centre

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Abstract

Background: Retinopathy of prematurity (ROP) is a multi-factoral vaso-proliferative retinal condition that affects mostly premature infants. In India, the prevalence of ROP in premature babies ranges from 35 to 60%. Some of the risk factors associated with ROP includes low gestational age, late onset of sepsis, low birth weight, blood transfusion and use of surfactants and intraventricular haemorrhage. Preventive measures are still lacking behind. Some of the clinical trials showed reduced oxygen dependency in preterm babies who were given vitamin A as preventive measures of ROP². Vascular endothelial growth factor (VEGF) demonstrated to have a role in pathogenesis of ROP, and Vitamin A may help prevent neovascularisation due to oxygen induced retinopathy, by down regulating VEGF expression thus deterring ROP onset.

Objective: To study the incidence of Retinopathy in preterms receiving Vitamin A.

Material & Methods: Institutional cross sectional study of 37 preterms with gestational age <34 weeks and birth weight <1750g were selected from January 2021 to November 2021. Consent of the mother or the father of the study participants were taken prior to including the infants in the study. All infants were started on oral Vitamin A supplement (5000 IU/oral on alternate days x 3 weeks), along with enteral nutrition once hemodynamically stable. The retinologist examines the infants after 3-4 weeks of birth or at 30-32 weeks of postconceptional age. First examination details were used to validate the findings, also the infants who had severe ROP; underwent laser therapy. Data was analysed by using the SPSS software and the incidence was then calculated.

Results: 11 out of 37 preterms on vitamin A supplementation developed some degree of ROP in one or both eyes (29.7%). Severity increased with decreasing gestational age. Based on the criteria of The International Classification for Retinopathy of Prematurity (ICROP), the disease reached stage 1, 2 and 3 in 2.7%(1), 8.1%(3) and 16.2%(6), respectively. No stage 4 and 5 ROP were detected.

Conclusion: The overall incidence of ROP in preterm who received Vitamin A supplementation was less by 29.7% when compared to the studies done earlier.-This shows that there is high likelihood of infants benefitting from Vitamin A supplementation in reducing Retinopathy of Prematurity.

Introduction

ROP is a multifactorial vaso-proliferative retinal disorder that increases in incidence with

decreasing gestational age. The condition is, by and large, limited to preterm babies with a birth weight of less than 1750 gram or gestational age

of less than 34 weeks. As the gestational age decreases, the incidence of ROP, a multifactorial vaso-proliferative retinal disorder increases. This is more often seen in preterm babies who weigh less than 1750 gram or whose gestational age is less than 34 weeks¹.

There is an approximate 25 million live births which happens in India out of which 8.5% of the births results in baby weighing less than 2 kg in weight. Incidence of ROP in the new born babies with weight less than 1750g lies between 35 to 60%. On the other hand, in 80% of the babies weighing less than 1000g are more vulnerable and are prone to develop ROP¹. Some of the risk factors which are associated with ROP include low gestational age, low birth weight, late onset sepsis, intra-ventricular haemorrhage, blood transfusion and the use of surfactants².

Vitamin A accounts to be one of the most important micro-nutrient which is needed for an orderly growth and differentiation in the infants. It is a fat-soluble vitamin and plays a vital role in regulating the growth of the epithelial cells as well as helps in the development of retina and lungs. It also plays a vital role in maintaining the normal vision^{3,4}.

The important role of vitamin A in the prevention of ROP is that it has the potential to reduce oxygen dependency in premature babies⁵. Vascular endothelial growth factor (VEGF) demonstrated to have a role in pathogenesis of ROP. Vitamin A may reduce neovascularisation caused by oxygen induced toxicity, by down regulating VEGF expression and so delaying ROP onset^{5,6}.

Plasma Vitamin A levels in preterm infants rise as the gestational age progresses⁷. As a result of limited transplacental transfer from their mothers, low intake through enteral feeding for several weeks after birth, and poor gastrointestinal absorption, puts the preterm babies at the risk for developing Vitamin A deficiency. According to a study, at least 65% of the infants with birth weight less than 1250g and 80% of the infants with a

birth weight of less than 1000g are at risk of developing some degree of ROP^{7,8}.

According to the International Classification of ROP (ICROP) 2005 guideline, ROP is classified in five stages in increasing stages of severity; the higher the stage of ROP, the more severe the disease is.⁹

Currently, there are no preventive measures adopted to tackle the given condition. Some of the studies suggests preventive measures, include erythropoietin, propranolol, caffeine, antioxidants and omega 3 poly unsaturated fatty acids; Vitamin A has been suggested to have a preventive effect on ROP¹⁰.

Some clinical trials have demonstrated the efficacy of vitamin A in the prevention of complications of prematurity, particularly ROP and BPD¹¹. In this article, we are studying the incidence of ROP in pre-terms receiving vitamin A supplementation.

Materials and Methods

This was a prospective observational study, conducted in the paediatric department of a tertiary care hospital. Neonates admitted in NICU were enrolled for the study as per the criteria given. It was a prospective, stratified randomized cohort study performed from January 2021 to November 2021. 37 preterm patients were selected. The Institutional Ethics Committee (IEC) approved the study. Written informed consent was obtained from both parents. Pre-terms with gestational age < 34 weeks and low birth weight babies <1750gram who were admitted in our NICU were selected for the study.

Inclusion Criteria

- 1) Preterms admitted <34 weeks gestation age.
- 2) Preterms < 72 hours of age
- 3) Receiving mechanical ventilation, non-invasive respiratory support or supplemental oxygen(fio2 >21%) at 24 hours of age.
- 4) Receiving oral Vitamin A supplementation (5000 IU on alternate days) .Started along

with enteral feeds as soon as infant is hemodynamically stable.

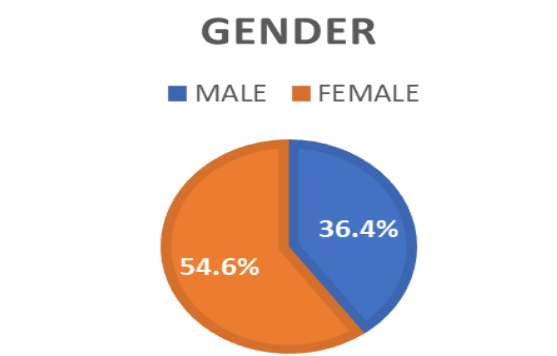
Exclusion Criteria

- 1) Congenital Major anomalies
- 2) Congenital TORCH infections with overt signs at birth
- 3) Genetic metabolic diseases.
- 4) Terminal illness as evidenced by pH <7.0 for > 2 hours or persistent bradycardia associated with hypoxia for >2 hours
- 5) Grade III or IV Intracranial hemorrhage

All infants born >28 weeks or > 1200g were screened at 3-4 weeks of chronological age. Preterms < 28 weeks of gestation or < 1200g were screened at 2-3 weeks. The retinologist was unaware about the vitamin A supplementation. The following examination was repeated based on the findings of the first examination. Infants with high grade ROP underwent laser therapy. Data was tabulated and analyzed using SPSS 20.0 version software.

Results

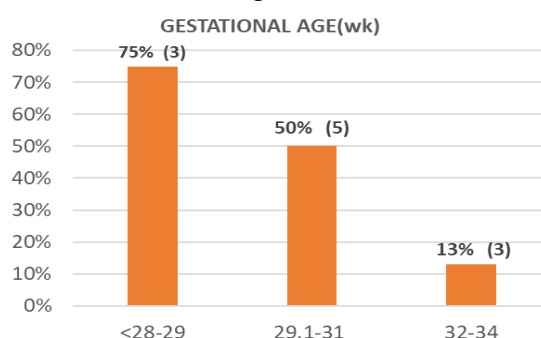
Figure 1: Gender Distribution of the studies cases



As per data collected, of 37 preterm on vitamin A supplementation, 11 infants were diagnosed to have ROP. Of which 6 were female (54.6%) and 5

were male (36.4%) who were screened for ROP. Male to female ratio 0.8:1.

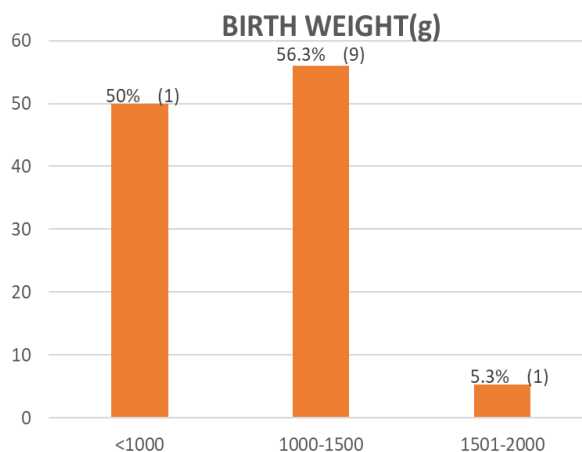
Figure 2: Relation between ROP and Gestational Age



Out of 37 preterms, 3 out 4 patients with gestational age <29 weeks developed ROP (75%).5 out of 10 babies (50%) between 29.1 to 31 weeks, and 3 out of 23 preterms (13%) between

32 -34 gestational age had developed ROP. Gestational age < 29 weeks was significantly associated with higher rates of ROP.

Fig 3: Birth weight and Retinopathy of prematurity



In this study, 1 (50%, 1 out of 2) infants less than 1000g had ROP. 9 pre-terms (56.3%, 9/16) between 1000-1500g and 1 preterm (5.3%, 1/19)

with birth weight >1501g developed ROP. The smallest infants with birth weight less than 1000g are at the highest risk.

Fig 4: Severity of ROP with Progressing Gestational age

Gestational age	Total Patients	ROP Patients	Stage 1	Stage 2	Stage 3	Plus Disease
<28-29 weeks	4	3(75%)			2	1
29.1 to 31 weeks	10	5(50%)		1	4	
32-34 weeks	23	3(13%)	1	2		
Total	37	29.7%	1	3	6	1

A total of 37 infants fulfilled the screening criteria. ROP was detected in 29.7% of neonates. 1 preterm (2.7%) had stage 1 disease, 3 infants (8.1%) with stage 2, 6 neonates (16.2%) with stage 3 ROP. Prethreshold disease was present in 1 (2.7%) preterm of gestational age 30.3 with birth weight of 1.49g. There were no cases with stage 4 and 5 ROP

Discussion

The present study was a hospital based prospective study conducted in the department of paediatrics of a tertiary care hospital. The total number of cases of preterm infants in the present study is 37 over the study period of 10 months. Out of the 37 premature patients, there were 11 infants diagnosed with varying stages of Retinopathy of Prematurity. Of which, there were

6 females and 5 male babies with male: female ratio of 0.8:1. Incidence was higher in infants with lower gestational age with 75% of preterms below 29 weeks showing ROP followed by 50% preterms between gestational age 29.1 to 31 weeks and 13% between 32-34 weeks showing ROP. Higher incidence may be attributed due to preterms having low body stores of Vitamin A as they have low levels of both retinol and retinol binding protein (RBP). Certain studies have shown association between low plasma vitamin A concentrations and development of ROP¹². In our study, association between birth weight and ROP was also evaluated. Incidence was 50% in infants below 1000g, 56.3% in preterms weighing between 1000-1500g and 5.3% in neonates between 1501 to 1750g. However, since gestational age is a major contributor of birth

weight, it was not possible to evaluate the independent effect of birth weight on ROP in the given study.

The study also shows increasing severity of ROP with decreasing Gestational age. Treatment was performed in all preterms with severe ROP(> stage 3) with regular follow up. The treatment involved laser photocoagulation.

The results of previous studies regarding incidence of ROP have varied. The overall incidence in India of ROP varies between 35 and 60% in babies weighing less than 1750g¹. Almost 80% of infants weighing less than 1000g are reported to develop ROP¹. This study was aimed to evaluate the incidence ROP in preterms on oral vitamin A supplementation. Certain studies have shown that parenteral/I.M administration of vitamin A is able to prevent complications of prematurity¹³. Oral formulation are well tolerated and no adverse events have been observed⁵. Certain studies have shown that parenteral administration of Vitamin A supplementation is able to prevent complications of prematurity¹³.

Overall incidence of ROP in preterms receiving Vitamin A supplementation was comparatively less i.e 29.7% as compared to results in the previously done studies.

Conclusion

In conclusion vitamin A supplementation is beneficial in reducing ROP in premature infants. As they have reduced body stores of Vitamin A and are at risk for developing vitamin A deficiency, therefore they should receive Vitamin A parenteral supplementation as early as possible within first few days of life. It may help in reducing the severity of ROP in extreme as well as incidence of Retinopathy of Prematurity.

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