

Original Research Article

Vitamin A supplementation for prevention of bronchopulmonary dysplasia in very low birth weight infants

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ABSTRACT

Background: Vitamin A maintains the integrity of epithelial cells of the respiratory tract and is an essential element for normal lung growth. The aim was to assess the effectiveness of vitamin A supplementation in very low birth weight (VLBW) infants to prevent development of bronchopulmonary dysplasia (BPD).

Methods: This was a retrospective cohort study to determine the effectiveness of vitamin A in preventing complications of prematurity in VLBW infants. Vitamin A was delivered intramuscularly at a dose of 5000 IU, three times weekly during the first 28 days of life.

Results: Of the 142 eligible VLBW infants, 60 VLBW infants received the vitamin supplement. We observed a significant difference between the groups in the duration of oxygen therapy or in the risk of bronchopulmonary dysplasia. Serum vitamin A levels were significantly raised in those who were supplemented.

Conclusions: Given the significant difference in development of BPD, days of oxygen therapy and days of ventilation, it is advisable to use Vitamin A supplementation in VLBW babies.

Keywords: BPD, Vitamin A, VLBW

INTRODUCTION

Vitamin A maintains the integrity of epithelial cells of the respiratory tract and is an essential element for normal lung growth.¹ Transfer of vitamin A to the fetus occurs throughout the pregnancy, and the accretion is maximum in the last trimester thus preterm neonates (especially those born before 32 weeks) are born with inadequate body stores of vitamin A.² Vitamin-A deficient normal infants show pathological changes in the lungs similar to that seen in bronchopulmonary dysplasia (BPD).¹

BPD is common in premature neonates with acute respiratory distress requiring prolonged mechanical ventilation and oxygen therapy.^{3,4} There has been hardly any change in the overall incidence of BPD over the past many years.^{5,6} Clinical trials suggest that vitamin A deficiency and alterations in vitamin A metabolism increases the risk of BPD in premature VLBW neonates.⁷

Furthermore, it has been hypothesized that treatment of the neonates prone to develop BPD with therapeutic doses of vitamin A can reduce the incidence of BPD.

This study is a retrospective analysis of data from the NICU of a tertiary care hospital to determine whether Vitamin A supplementation in preterm VLBW babies reduces the risk of development of moderate to severe BPD. The difference in mortality, total number of days of mechanical ventilation and oxygen supplementation, with patients who did not receive vitamin A supplementation were also compared.

METHODS

Retrospective analysis of records of all neonates in a neonatal intensive care facility of a tertiary care hospital of Eastern UP, admitted between June 2012 - May 2013 weighing <1500 gm, < 32 weeks, appropriate for

gestational age, without any major congenital anomaly, in need of oxygenation/mechanical ventilation at 24 hours of age was done. The children who died in the first 4 weeks of life or 36 weeks corrected gestational age were excluded from the study. All critically ill new-born severe sepsis, congenital anomaly, trauma during birth, meconium aspiration pneumonia and those thought to have terminal illness (pH <7.0, presence of hypoxia with bradycardia for >2 hours) were excluded from further analysis.

Among those analysed, neonates who were given intramuscular Vitamin A in doses of 5000 IU thrice weekly upto 28 days of life along with supportive management were compared with those who did not receive Vitamin A at all. Its use is indicated in all VLBW infants who require a fraction of inspired oxygen exceeding 21% on admission. BPD was defined according to the criteria of Jobe et al, oxygen requirement >21% at 28 days of age and/or >21% positive pressure in the airway at 36 weeks corrected gestational age.⁴ During the period of administration of vitamin A, plasma levels of vitamin A were determined by liquid chromatography at admission and 28 days of life.^{8,9}

All infants included in the study were managed according to the NICU guidelines. The study was approved by the hospital ethics committee and informed consent was obtained from the parent or guardian of the patients for

the use of their data. The statistical analysis consisted of a descriptive analysis, a comparison of the means test for independent samples, and chi-square analysis for categorical variables.

RESULTS

From June 2008 to May 2009, 202 VLBW infants were treated in NICU. 60 neonates were excluded from the study as per exclusion criteria. Baseline perinatal data are shown in Tables 1. No perinatal differences were observed between the infants who received vitamin A and those who did not.

Table 1: Perinatal data, mean (SD), for infants given supplementary vitamin A and untreated infants.

	Vitamin A +	Vitamin A -
Patients (no.)	60	82
Gestational age (weeks)	30.1 (1.5)	29.8 (1.9)
Birth weight (gms)	1324 (159)	1304 (135)
Female infants (n %)	24 (40)	34 (41.46)
LSCS n%	16 (26.67)	22 (26.83)
Completed course of antenatal steroids (n%)	35 (58.33)	40 (48.78)
Surfactant (n%)	05 (8.33)	07 (8.53)

*P ≤ 0.05; SD = Standard deviation

Table 2: Clinical results for infants given supplementary vitamin A and untreated infants.

Results	Vitamin A+	Vitamin A-
Days in NICU (SD)	32 (10.4)	30 (12.6)
Bronchopulmonary dysplasia n (%)	3 (5.00)	15 (18.29)* (4.25;1.17-15.43)
Mild	2 (3.33)	11 (13.41)* (4.493;0.95-21.08)
Moderate	1 (1.67)	5 (6.09)
Severe	-	-
Serum retinol at admission (mg/dl)	16.38 (13.11)	15.92 (23.13)
Serum retinol at 28 days (mg/dl)	62.15 (14.25)	18.28 (26.22)**
Mortality n (%)	3 (5)	11 (13.41)
Mean duration of oxygen therapy (SD)	18.31 (18.88)	26.71 (24.56)*
Mean duration of mechanical ventilation (SD)	5.37 (6.12)	11.48 (14.56)**

*P < 0.05; **p < 0.005

As shown in Table 2, there is a statistically significant differences in the prevalence of BPD between the infants who were given vitamin A and those who were not (odds ratio 4.25 ; 95% confidence interval (CI):1.17-15.43). Serum levels of vitamin A were 62.15 mg/mL (standard deviation (SD):26.22) in the patients with BPD and (SD: 18.28) in those with no BPD, and there was a highly significant difference between the groups. Infants given vitamin A supplementation received oxygen treatment for significantly lesser periods to those for the infants who were not supplemented. The numbers of days for mechanical ventilation were also significantly less among infants given the vitamin A supplement. With respect to

the number of days of stay in the ICU no significant difference could be ascertained between two groups. Mortality in both groups was similar. No clinical manifestations attributable to vitamin A toxicity in any of studied patients such as bulging fontanelles, vomiting, diarrhoea, loss of appetite and irritability was observed.^{10,11}

DISCUSSION

This retrospective data in 142 neonates demonstrated the benefits of Vitamin A supplementation in VLBW babies. The study shows that babies supplemented with Vitamin

A have significantly lesser chances of development of BPD. Efficacy of vitamin A in the prevention of BPD that has been demonstrated by some authors in experimental models.^{12,13} The pathogenesis of BPD involves the factors causing injury to an immature lung and factors inhibiting its healing. Vitamin A is an essential micronutrient for regeneration of injured epithelial cells.¹ Mean duration of oxygen supplementation and days for mechanical ventilation in babies who were given Vitamin A supplement was also significantly less, which is similar to findings of Shenai et al.² Few studies, however, also demonstrate that there is no benefit in development of BPD or duration of oxygen therapy, they attribute this decline be coincident with improved ventilatory techniques with guaranteed volume utilization and a more rational use of oxygen therapy but also with increased nutritional inputs of protein and energy, as recommended by the ESPGHAN.¹²⁻¹⁵ Difference in mortality among both groups was not seen which is similar to the findings of Uberos et al.¹² Dose for supplementation of vitamin A was safe and no side effects were demonstrable.

Thus it can be concluded that vitamin A supplementation in VLBW babies is beneficial in bringing down the incidence of BPD and the number of days of oxygen therapy and mechanical ventilation. A regular supplementation in such babies will not only bring about a decrease in incidence of BPD but also reduce the morbidity and cost of therapy by reducing the number of days of oxygen therapy and mechanical ventilation. Some recent studies have also demonstrated the beneficial effects of Vitamin A supplementation in prevention of Retinopathy of prematurity, intraventricular hemorrhage, sepsis etc.^{16,17} Larger randomized trials are required to explore these benefits.

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