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Original Article

Is there a potential link between vitamin D and pulmonary morbidities in preterm infants?

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Abstract

Background: There hasn't been conclusive proof about the association between vitamin D and pulmonary morbidities of prematurity.
Methods: 106 preterm infants were retrospectively included into this study. Clinical data and blood samples of all the patients were collected within 24 h of admission.
Results: (1) Respiratory distress syndrome (RDS) patients were mainly concentrated in "≤30 weeks" stage when compared with other two gestational age groups. The only significant decrease of vitamin D concentration between RDS and non-RDS patients reflected in "≤30 weeks" stage (RDS *vs.* non-RDS: 29.48 ± 13.06 *vs.* 40.47 ± 20.52 nmol/l). (2) Bronchopulmonary dysplasia (BPD) patients were also concentrated in "≤30 weeks" stage. Vitamin D concentration showed significant difference both in "≤30 weeks" stage and "30−34 weeks" stage (≤30 weeks stage, BPD *vs.* non-BPD: 33.20 ± 16.51 *vs.* 39.21 ± 16.65 nmol/l; 30−34 weeks stage, BPD *vs.* non-BPD: 30.36 ± 15.50 *vs.* 41.21 ± 20.40 nmol/l). (3) Though vitamin D concentration in mechanical ventilation (MV) group was lower than non-MV group, there're no significant differences. (4) Vitamin D concentration in dead cases was significant lower than survival patients at discharge. (5) It showed a good correlation between vitamin D concentration and serum Ca, serum P, duration of MV and duration of oxygen support in "≤30 weeks" stage.
Conclusion: The significant decrease of vitamin D concentration between RDS and non-RDS patients only reflected in "≤30 weeks" stage. And significant decrease of vitamin D concentration in BPD patients was both showed in "≤30 weeks" stage and "30−34 weeks" stage, which is consistent with "duration of oxygen support". However, the overall effect did not show any difference in all preterm infants. It seems that the appropriate concentration of vitamin D is beneficial to lung maturation of human. Certainly, large sample, multi-center randomized controlled trials are necessary.

Keywords: BPD; Preterm infants; RDS; Vitamin D

1. Introduction

The importance of vitamin D in newborn and child health has been increasingly recognized in the last several years.[1,2] Furthermore, vitamin D seems to play a role in embryogenesis, cellular growth and differentiation, including the regulation of lung development and lung maturation in the fetus.[3−5] So, the impact of vitamin D on lung development and pulmonary diseases of early life has attracted more and more attention of neonatologists.

Respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD) are major pulmonary complications to preterm infants. To date, the most dramatic improvement in treating RDS is intratracheal surfactant and mechanical ventilation, leading to decreased mortality and morbidity.[6]

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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However, despite improved treatment techniques, RDS is still a severe, high-mortality disease in the extremely premature infant. In survivors, a considerable part of preterm infants may be accompanied by BPD, a chronic lung disease characterized by impaired alveolar development and inflammation response.[7] In fact, many preterm infants, especially extremely low birth weight babies need oxygen support for a long time after birth in routine clinical practice.

Vitamin D deficiency is common among infants, and pregnant and lactating mothers in the worldwide.[8,9] Among the population of newborns, preterm babies often have less vitamin D stores due to less sunlight exposure and decreased trans-placental transfer from deficient mothers, and consequently have a higher requirement.[10,11] Animal and laboratory studies have showed substantial positive effects of vitamin D on the alveolar type II cell (ATII), fibroblast proliferation, surfactant synthesis, and alveolarization.[3,12,13] These data support the hypothesis of hypovitaminosis D as a frequent, modifiable risk factor of RDS and BPD. However, the evidence of an impact of vitamin D on human fetal and neonatal pulmonary diseases has still been sparse.[14] KE Joung et al.[15] once found that low 25(OH)D level is frequent and modifiable among preterm infants at birth. However, they didn't detect any association between vitamin D status and pulmonary or other morbidities of prematurity.

In view of such an uncertain situation, clinical data of 106 preterm infants from our center were analyzed retrospectively. And we hope that this paper could add some persuasive evidences to clinical application of vitamin D in preterm infants.

2. Methods

2.1. Preterm infants

(1) Inclusion criteria: from January 2015 to January 2016, we retrospectively selected (By random number table method to avoid selection bias) 106 preterm infants (Gestational age <37 weeks) admitted to Children's Hospital of Nanjing Medical University, a representative level III NICU in East China. (2) Exclusion criteria: infants with severe congenital malformations, severe infection, inherited metabolic diseases, give up treatment within 24-h after birth. (3) Diagnostic criteria of BPD: BPD is defined as a requirement for oxygen at 36 weeks' corrected gestational age.[16,17] Diagnostic criteria of RDS: RDS is defined according to the latest guideline – 2016 European Consensus Guidelines on the Management of Respiratory Distress Syndrome.[18] (4) Ethics: This retrospective observational study was approved by the hospital ethics committee (Number: NJCH2016003) and informed consent was obtained from the patient's guardians.

2.2. Collecting methods

(1) All enrolled infants were admitted to hospital within 24 h after birth to collect the routine clinical data and blood samples. Clinical data contain: mother's age, birth weight, gestational age, admission age, gender, Apgar score, clinical diseases and respiratory support. Blood samples were collected, comprising: vitamin D concentration, serum calcium and serum phosphorus. (2) Blood samples collection method: Take fasting peripheral venous blood 2 ml within the age of 24 h, saved in procoagulant tube. 25(OH)D (Represented as vitamin D) level was measured by automatic biochemical analyzer (Type 1024, Tokyo), showing as nmol/l.

2.3. Statistical methods

Statistical analysis was performed using SPSS 13.0 software. Quantitative data were showed as mean ± standard deviation. Between the two groups were compared using *t* test, and among more than two groups were compared using analysis of variance. Pearson correlation coefficients between the variables were calculated. For qualitative data, Pearson chi-square test (or fisher exact probability method) were performed. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Analysis of baseline data

This study finally included 106 preterm infants, and newborns between 30 and 34 weeks occupy the majority of the proportion. Mothers' age gradually decreased with gestational age increasing ($P < 0.05$), while vitamin D concentration increased gradually with gestational age. But there're no significant differences in gender, admission age, Apgar score, serum Ca and serum P among different gestational age groups (Shown in Table 1).

3.2. Comparison of vitamin D concentration between RDS and non-RDS, BPD and non-BPD, mechanical ventilation (MV) and non-MV, death and survival

(1) RDS patients were mainly concentrated in "≤30 weeks" stage (11/15, 73.3%) compared with other two gestational age stages (Shown in Table 1). The only significant decrease of vitamin D concentration between RDS and non-RDS patients reflected in "≤30 weeks" stage (RDS *vs.* non-RDS: 29.48 ± 13.06 *vs.* 40.47 ± 20.52 nmol/l) ($P < 0.05$) (Shown in Table 2).

(2) BPD patients were also concentrated in "≤30 weeks" stage (3/15, 20.0%) compared with other two gestational stages (Shown in Table 1). Vitamin D concentration showed significant difference between BPD and non-BPD patients both in "≤30 weeks" and "30–34 weeks" stages (≤30 weeks, BPD *vs.* non-BPD: 33.20 ± 16.51 *vs.* 39.21 ± 16.65 nmol/l; 30–34 weeks, BPD *vs.* non-BPD: 30.36 ± 15.50 *vs.* 41.21 ± 20.40 nmol/l) ($P < 0.05$) (Shown in Table 2).

(3) Though vitamin D concentration in MV group was lower than non-MV group, there're no significant differences ($P > 0.05$) (Shown in Table 2).

(4) It has a higher mortality in the "≤30 weeks" group ($P < 0.01$) (Shown in Table 1). And vitamin D concentration

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