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The Frequency of Early and Late Hypocalcemia Among Hospitalized Newborns in An Iranian Hospital

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Background: Hypocalcemia is a common neonatal abnormality particularly in high-risk neonates. Hypocalcaemic neonates with early diagnosis recover after a period of treatment with calcium.
Objectives: In this study we aimed to determine the frequency of early and late hypocalcemia, as well as the influence of some relating factors.
Patients and Methods: One hundred neonates with early or late hypocalcemia (hospitalized in Aliasghar Hospital of Tehran, Iran, during 2011) were enrolled. The required information was extracted from medical records. The frequency of each hypocalcemia type and relating factors were assessed.
Results: Amongst all subjects, 63% had early and 37% had late hypocalcemia. We found significant associations between early or late hypocalcemia with Apgar score of < 5 and prematurity ($P < 0.05$).
Conclusions: Calcium supplemented food could prevent hypocalcemia complications in high-risk neonates.

Keywords: Hypocalcemia; Newborns; Apgar Score; Premature

1. Background

Hypocalcemia is a common neonatal abnormality particularly in high-risk neonates including infants of mothers with diabetes, infants with perinatal asphyxia, and premature and preterm infants. Calcium has crucial roles in many biochemical processes, such as blood coagulation, neuromuscular excitability, cell membrane integrity and cellular enzymatic activities. Its normal range at different ages has been reported to be between 8.8 and 10.6 mg/dl. Neonatal hypocalcemia is defined as serum or plasma tCa of < 2 mmol/L (8 mg/dL) in term and tCa of < 1.75 mmol/L (7 mg/dL) in preterm infants. Early onset Neonatal Hypocalcaemia (ENH) presents within the first three days of life, in contrast to late onset hypocalcemia, which usually presents after 72 hours (1-3).

The etiology of neonatal early onset hypocalcemia includes prematurity, neonatal asphyxia, intrauterine growth retardation (IUGR), maternal complications such as diabetes, anticonvulsant drugs and hyperparathyroidism while in late onset hypocalcemia these causes are hypoparathyroidism, phototherapy, hypomagnesemia, gastroenteritis due to Rota virus, and high phosphate intakes or vitamin D deficiency (4, 5).

Although there have been some studies over the past few years looking at the frequency of neonatal hypocalcemia in Iran (6, 7), there is a lack of information regarding the different types of neonatal hypocalcemia and the relating factors. Such investigation would be beneficial for health organizations to set plans and proper strategies to decrease neonatal morbidity due to hypocalcemia and consequently neonatal hospitalization period.

2. Objectives

The purpose of the present study was to determine the frequency of early or late neonatal hypocalcemia at Aliasghar hospital during a one-year period.

3. Patients and Methods

During 2011 - 2012 a cross-sectional retrospective study was carried out at Aliasghar Hospital, a tertiary referral center and also one of the teaching hospitals affiliated to Iran University of Medical Sciences (Tehran, Iran). Of all hospitalized neonates at the Neonatal Intensive Care Unit (NICU) and nursery ward during the one-year period of the study, 100 newborns had hypocalcemia (based on medical records). The exclusion criteria were infants with missing or incomplete data and infants older than 28 days. We divided our subjects to two groups based on on-

set of hypocalcemia; group A, early onset (during the first three days of life) and group B, late onset (after 72 hours). All demographic data related to neonates and their mothers including sex, birth weight, gestational age, Apgar one minute score, Apgar five minute score, neonatal complications, type of delivery, type of hypocalcemia and symptoms, maternal age, parity, and prenatal problems were recorded. Next, we determined the frequency of hypocalcemia (early and late) and evaluated the influence of some relating factors.

Informed consent was obtained from each participant. Patients' data were kept confidential. Ethics approval for the study was obtained from the institutional review board of Iran University of Medical Sciences.

All data were analyzed with the SPSS software (version 17). T-tests, chi-square and Fisher's test were used where applicable. P of ≤ 0.05 was considered statistically significant.

4. Results

Of the 100 neonates, 61 neonates were male, and 63 cases (63%) had early hypocalcemia with mean weight of 2342.38 ± 898.39 g, while 37 (37%) had late hypocalcemia with mean weight 2540.54 ± 0.86 g. Of all mothers 63% (mean age of 25.20 ± 4.89) delivered their infants through Cesarean Section (CS) and 37% (mean age of 24.69 ± 4.87) had gone through Natural Vaginal Delivery (NVD). Mean maternal parity of group A was 1.93 ± 1.2 while for group B this was 1.54 ± 0.86. Four mothers had Gestational Diabetes Mellitus (GDM) and one had epilepsy. We evaluated the magnesium level of 18 neonates because of doubt in hypomagnesemia, of which seven cases (38.8%) had hypocalcemia and hypomagnesemia, simultaneously. In early hypocalcemic neonates, 15% and 4% showed seizure and muscle twitch while in late hypocalcemic cases these clinical manifestations were 5% for seizure and 5% for muscle twitch.

We found a positive association between low first minute Apgar score (< 5) and both early or late hypocalcemia presentation (P = 0.025, P = 0.025). Moreover, early or late hypocalcemia was more frequent in premature infants (P = 0.004, P = 0.04).

Diabetes had a significant influence on frequency of hypocalcemia in our hospitalized subjects (P = 0.039), however this finding may not be reliable due to the small number of mothers with diabetes in this study.

No significant relationships were seen between frequency of hypocalcemia and neonatal weight, gender, sepsis, kernicterus, blood exchange, photo-therapy or maternal age and type of delivery.

5. Discussion

Hypocalcemia was a common clinical and laboratory problem observed in our neonates. Late diagnosis causes complications such as cardiopulmonary dysfunction, hypocalcemic seizure and tetany, which increase neonatal morbidity and mortality (8, 9). The aim of the present study was to determine the frequency of early and late hypocalcemia in hospitalized neonates and assess its associated factors. This report shows the importance of the evaluation, early detection and treatment of hypocalcemia in neonates to prevent subsequent serious complications.

Early hypocalcemia was more frequent than late hypocalcemia in our population (63% vs. 37%). Based on its etiology this frequency may diminish dramatically by some efforts; for instance sooner diagnosis and treatment of mothers with greater risk of diabetes, anticonvulsant drug and hyperparathyroidism may help physicians prevent neonatal early hypocalcemia. Consistent with our results Jain et al. confirmed that late neonatal hypocalcemia is rare as compared to early hypocalcemia (3).

We found that early and late hypocalcemia were more common in neonates with one minute Apgar score of five or less. Birth asphyxia plays a critical role in neonatal calcium homeostasis. Neonatal asphyxia causes hypocalcemia by effects on calcium absorption, phosphorous concentration, calcitonin, parathormon status and infants' oral intake (10). In accordance to our results, Jain et al. confirmed that infants with perinatal asphyxia had lower serum Calcium (3).

Based on our results, early or late hypocalcemia were more frequent in premature infants. Premature termination of trans-placental supply, exaggeration of the postnatal drop to hypocalcemic level, increased calcitonin and decrease target organ responsiveness to parathyroid hormone are considered as associated factors. A high percentage of hypocalcemia was detected in premature infants from 28 to 32 gestational weeks (3).

Mothers' diabetes also influenced the frequency of hypocalcemia in our hospitalized subjects; this may due to higher calcium demand by the macrosomic fetus or maternal fetal hypomagnesemia resulting hypoparathyroidism and hypocalcemia. Alam et al. showed high frequency of complications such as hypoglycemia and hypocalcemia in neonates of mothers with diabetes (11). In one study, hypocalcemia was observed in 17% of neonates whose mothers had gestational or pregestational diabetes (12).

We also found that seizure was the most common symptom in early and late hypocalcemia and this finding was consistent with other previous studies (13, 14). Cakir et al. (9) also reported that neonatal hypocalcemia may present different symptoms such as hypotonia, poor feeding, stridor, and jitteriness, yet the most alarming symptom was the seizure activity.

Finally we found that amongst the 18 neonates with doubt in hypomagnesemia, seven cases (38.8%) had hypocalcemia and hypomagnesemia, simultaneously. A previous investigation has indicated that neonatal hypomagnesemia can induce hypoparathyroidism resulting hypocalcemia (3). Visudhiphan et al. also showed hypomagnesemia with secondary hypocalcemia in their study (15).

Our study had some limitations. Firstly, our sample size was small thus we could not evaluate more maternal complications. We also did not consider other factors such as Vitamin D status or maternal calcium level as other associated factors and we suggest that these variables should be considered in future studies.

As hypocalcemia in our population was more frequent, calcium supplemented food should prevent hypocalcemia complications in high-risk neonates.

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Authors' Contributions

Nasrin Khalesi designed and coordinated the study and participated in most of the experiments. Parva Namiranian and Sara Samavati coordinated and carried out all the experiments, analyzed the data and participated in manuscript preparation. Zahra Farahani provided assistance for all experiments and prepared the manuscript. All authors read and approved the content of the manuscript.

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