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ORIGINAL ARTICLE

Renal Calcification in Very Low Birth Weight Infants

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Key Words
lithiasis;
nephrocalcinosis;
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Background: Renal calcification in preterm infants has been described frequently. The etiologic factors have not yet been fully clarified. The objective of this study was to evaluate the incidence of and risk factors for renal calcification in our population.
Methods: We retrospectively reviewed the charts of very low birth weight preterm infants during a 1-year period. Renal ultrasound scans were performed at term or before discharge and at a corrected age of 1 year.
Results: Six infants (6%) had renal calcification at term or before discharge compared with 96 who did not. Factors significantly associated with renal calcification included gestational age (26 weeks *vs.* 29 weeks, $p = 0.006$), birth weight (851 g *vs.* 1141 g, $p = 0.004$), duration of mechanical ventilation (69 days *vs.* 29 days, $p = 0.002$), length of intensive care (72 days *vs.* 41 days, $p = 0.013$), furosemide therapy (33% *vs.* 3%, $p = 0.027$), and dexamethasone therapy (50% *vs.* 2% $p = 0.001$). Birth weight and dexamethasone therapy had significant independent association after stepwise logistic regression analysis. Sex, oliguria, acidosis, duration of oxygen therapy, length of hospital stay, nutrition status, and nephrotoxic drugs did not differ between the two groups. Three of the six infants had spontaneous remission of renal calcification, whereas two patients without the finding in neonatal stage had renal calcification at a corrected age of 1 year.
Conclusion: The incidence of renal calcification in very low birth weight infants in this study was relatively low, and the calcification was transient in one-half of the infants. Extremely premature, sick infants requiring long-term ventilation, and those receiving furosemide or

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dexamethasone were more likely to have renal calcification. Clinicians should be aware that renal calcification may develop beyond the neonatal stage.

1. Introduction

Renal calcification, including nephrocalcinosis and nephrolithiasis, is well recognized in adults but is also increasingly seen in preterm infants. Since first reported in 1982 by Hufnagle et al,[1] nephrocalcinosis has been thought by a number of investigators to be a complication of prematurity, very low birth weight (VLBW) infants being particularly vulnerable.[2–9] The reported incidence has ranged from 10% to 65%, depending on the study population, screening criteria, and ultrasound equipment used.[2–9] The etiology of renal calcification has not yet been fully clarified, but a multifactorial origin is likely.[10] Furosemide therapy has been proposed as a risk factor because of its hypercalciuric effect.[11,12] Other factors, such as low gestational age; low birth weight; prolonged oxygen dependency; imbalance in urine or serum chemistry; and treatment with corticosteroids, xanthines, and nephrotoxic drugs, may also contribute to renal calcification.[2–14] A small study from the United States found that white infants were more likely than nonwhites to have nephrocalcinosis,[15] suggesting there may be ethnic differences. There is also debate about the prognosis of nephrocalcinosis, as both spontaneous resolution without sequelae and ongoing renal tubular dysfunction have been reported.[16–20] The objective of this retrospective study was to evaluate the incidence and risk factors of renal calcification in our population of VLBW infants over the course of 1 year. As far as we are aware, this is the first study of renal calcification in premature Taiwanese infants.

2. Materials and Methods

We retrospectively reviewed the charts of all premature infants with a birth weight below 1500 g and a gestational age of less than 34 weeks who were hospitalized in the neonatal intensive care unit (NICU) of Taipei Mackay Memorial Hospital from July 2007 to June 2008. Patients who died before discharge or had major congenital malformations were excluded, as were infants who were not born at our hospital or who did not have renal ultrasonography during hospitalization. This study was approved by the ethics and medical research committees in our hospital.

Based on a clinical impression that renal calcification was relatively common among premature infants, in July 2007, we established the practice of performing routine renal ultrasound scans at term or before discharge in all VLBW preterm infants. The diagnosis of renal calcification included nephrocalcinosis and nephrolithiasis, using criteria described by Myracle et al.[21] Nephrocalcinosis was defined as focal areas of hyperechogenicity within the renal cortex, and nephrolithiasis was defined as calculus located in the collecting system. Patients were examined in the supine and prone positions. All scans were performed by one experienced nephrologist using ALOKA SSD-1700 equipment with a 5 MHz transducer (Aloka Co. Ltd., Wallingford, Conn., USA), and all scan photographs were reviewed by another nephrologist. If renal calcification was detected, renal ultrasound was performed monthly until resolution. All infants had a follow-up scan at a corrected age of 1 year, regardless of whether calcification had been noted on the initial scan.

For this study, a number of variables were compared between infants with and without renal calcification. Demographic characteristics assessments included gestational age, birth weight, Apgar score, and gender. Oliguria was defined as urine output of less than 1 mL/kg/d in 24 hours and acidosis as an arterial blood pH less than 7.2. All infants were fed with either the mother's milk or preterm infant formula. When oral alimentation reached 100 mL/kg, human milk fortifier was added. Most infants received parenteral nutrition before full feeding was established. The number of days of parenteral nutrition, formula feeding, and breastfeeding were recorded. Infants who required oxygen support at a postconceptional age of 36 weeks and who had chest X-ray changes were defined as having chronic lung disease (CLD). The duration of mechanical ventilation, oxygen therapy, and length of NICU and hospital stay were recorded, as were all medications with dosage and duration of use.

If renal calcification was detected, blood and spot urine samples were taken and assayed by standard laboratory methods. Serum chemistry studies included calcium, phosphate, and creatinine. Random urine specimens were collected in attached plastic bags and routine urinalysis performed and calcium, phosphate, and creatinine levels measured. The urinary calcium to creatinine ratio was calculated; a value higher than 0.8 mg/mg was counted as hypercalciuria.[22]

For statistical analysis, Fisher's exact test was used for nominal parameters and *t* test was used for continuous parameters. A *p* value less than 0.05 was considered statistically significant. Regarding the correlation of all parameters, Pearson's correlation coefficient was used for comparing two continuous parameters. Eta-squared correlation ratio was used for nominal by continuous parameters and lambda coefficient was used for nominal by nominal parameters. Stepwise forward Wald method was used in the multivariate logistic regression to select independent variables. The parameters entry and removal criteria was *p* value less than 0.05 and more than 0.10, respectively. All of the statistical calculations were performed using the SPSS 17th edition for Windows XP (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Neonatal stage

During the 1-year study period, 121 surviving VLBW infants with a gestational age of less than 34 weeks were hospitalized