Metabolic Bone Disease of Prematurity

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Metabolic bone disease of prematurity (MBDP) is a significant health risk with an incidence of approximately 20% in very low birthweight (VLBW) infants and up to 60% in extremely low birthweight (ELBW) infants in many neonatal units, despite an increasing awareness of its contribution to overall morbidity and protocols to reduce its incidence. The provision of adequate nutrients to very preterm infants in the first weeks of life to prevent increased morbidity (such as poor neurological development, impaired growth, bronchopulmonary dysplasia, retinopathy of prematurity, and metabolic bone disease) is a complex strategy [1]. In this issue of Indian Pediatrics, Pournami and colleagues [2] report on a prospective study aimed at reducing the incidence of MBDP in very low birthweight infants with gestational ages of ≤30 weeks by early monitoring of serum phosphorus and supplementation with intravenous and/or oral phosphorus from day 4 of life. Once enteral feeding rates (human milk) of 40 mL/kg/day were achieved, a human milk fortifier was progressively introduced. Overall, the rate of MBDP ranged from 2.8% in those infants with gestational ages between 28-30 weeks to 69.2% in those with gestational ages ≤26 weeks [2]. The overall incidence was considered by the authors to be less than that found in their earlier study in which attention to early phosphorus supplementation was less stringent; the results obtained thus encourage the authors to promote early mandatory use of phosphorus supplements [2].

Although, phosphorus deficiency is recognized as a major player in the pathogenesis of MBDP, perturbations in calcium homeostasis and vitamin D status may also play significant roles, together with serum phosphorus concentrations. Serum phosphorus needs to be monitored carefully during the first few months of life in very preterm infants, especially in those who have respiratory and gastrointestinal complications or who have been on methylxanthines, diuretics or corticosteroids. Researchers have cautioned about the risk of increasing MBDP through stimulating secondary hyper-parathyroidism when low birthweight infants are supplemented with phosphorus supplements alone [3]. In a recent study [4], parathyroid hormone (PTH) concentrations were found to be elevated at a mean of 15 days post-delivery in 40.3% of neonates with gestational ages <32 weeks. Perhaps, not surprisingly, PTH levels did not correlate with MBDP, when the latter was diagnosed using elevated alkaline phosphatase levels and hypophosphatemia, but they were inversely related to gestational age and urinary Ca/Cr ratios. Furthermore, PTH levels were found to be elevated in over 80% of ELBW neonates who were diagnosed with osteopenia on radiographs [5]. These findings indicate that inadequate retention of calcium also plays a major role in MBDP, despite few neonatal units monitoring PTH routinely in very premature infants (in the USA only 1.7% of units monitor PTH routinely).

Even though the role of vitamin D in phosphorus and calcium intestinal absorption in the first few weeks of life is unclear [6], it is important that vitamin D deficiency in the neonate be prevented. Thus, vitamin D supplementation of pregnant mothers should be considered a priority in those countries where maternal vitamin D deficiency is common, so as to ensure neonatal vitamin D sufficiency. Infants born to mothers who are vitamin D deficient, are likely to be vitamin D deficient as neonatal 25-hydroxyvitamin D (25(OH)D) concentrations are generally about 80% of maternal levels. With a half-life of approximately 21 days, 25(OH)D levels in the neonate fall rapidly unless vitamin D supplementation begins as soon as the infant is taking enteral feeds successfully. Although, some neonatologists recommend vitamin D supplementation of premature infants at levels (800-1000 IU/day) greater than those recommended for full-term infants (400 IU/day), there is little evidence to suggest that these higher levels are required unless there is hepatic or intestinal dysfunction. The use of activated vitamin D (calcitriol or alfacalcidol) has not been shown to have advantages over the use of the parent vitamin D, except possibly in situations of severe kidney or liver disease. The
need for close monitoring of vitamin D status with frequent measurements of serum 25(OH)D, which is costly, is unnecessary if there are no contraindications to routine vitamin D supplementation.

In order to assess the efficacy of early phosphate supplementation (within 4 days of life) in the prevention and management of MBDP and in reducing the other complications such as growth retardation in VLBW and ELBW infants, there is a need for more formal assessments through randomized controlled trials, monitoring not only serum phosphorus, but also other disturbances in bone mineral homeostasis.

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REFERENCES