Maternal calcium metabolism and bone mineral status

Ann Prentice

ABSTRACT Human pregnancy is associated with major changes in calcium and bone metabolism and in bone mineral status before and after gestation. The changes are compatible with the uptake and mobilization of calcium by the maternal skeleton to meet the high requirement for fetal growth and for breast-milk production. Breast-feeding is accompanied by decreases in bone mineral status, increases in bone turnover rate, and reductions in urinary calcium excretion. These effects are reversed during and after weaning, and, in several skeletal regions, bone mineral content ultimately exceeds that measured after delivery. By 3–6 mo after lactation, the postpartum changes in bone mineral status of women who breast-feed largely match those of women who do not, regardless of the duration of lactation. No consistent picture has emerged of the effect of pregnancy on bone mineral status, although increases in bone turnover, calcium absorption, and urinary calcium excretion are well recognized. Events before conception may modify the bone response, particularly if conception occurs within a few months of a previous pregnancy or lactation. There is no evidence that the changes observed during lactation reflect inadequacies in calcium intake. Supplementation studies have shown that neither the bone response nor breast-milk calcium secretion is modified by increases in calcium supply during lactation, even in women with a low calcium intake. The situation in pregnancy is less clear. Calcium nutrition may influence the health of the pregnant woman, her breast-milk calcium concentration, and the bone mineralization and blood pressure of her infant, but these possibilities require formal testing. Am J Clin Nutr 2000; 71(suppl): 1312S–6S.

KEY WORDS Bone mineral, breast-feeding, calcium, lactation, pregnancy, women, supplementation

INTRODUCTION

Profound changes in calcium metabolism and bone mineral status accompany human pregnancy both during gestation and after delivery. Accumulating data suggest that these changes are largely reversible and are independent of maternal dietary calcium intake. The patterns of change are compatible with the hypothesis that physiologic, homeorrhetic mechanisms exist to ensure an adequate supply of calcium for fetal growth and breast-milk production without reliance on an uninterrupted input from the maternal diet. This report summarizes the body of evidence, with particular emphasis on recent studies from several research groups that have led to the developments in current thinking, and discusses the implications of these findings for public health and for future research priorities.

CALCIUM METABOLISM

Calcium absorption and urinary calcium excretion are higher during pregnancy than before conception or after delivery (1–5). The increases are evident in early-to-mid pregnancy and precede the increased demand for calcium by the fetus for skeletal growth. Bone resorption is also elevated, as indicated histologically (6) and biochemically by measurements of plasma markers such as tartrate-resistant acid phosphatase and the urinary excretion of collagen cross-links, telopeptides, or hydroxyproline (4, 5, 7). The increase in resorption rate is apparent by early gestation and rises further during pregnancy (4, 5, 8). Bone formation increases similarly, as indicated by plasma markers such as bone alkaline phosphatase and procollagen peptides (4, 8). However, osteocalcin concentration, a commonly used plasma marker of bone formation, is lower throughout pregnancy than before conception (4, 5), although concentrations in late gestation are higher than those earlier in pregnancy (4, 5, 8). This may be due to uptake of osteocalcin by the placenta (9). The alterations in calcium and bone metabolism during pregnancy are accompanied by increases in the calcitropic hormone 1,25-dihydroxyvitamin D (calcitriol) but with little discernible alteration in either intact parathyroid hormone or calcitonin concentrations (4, 5).

After delivery, calcium absorption and urinary calcium excretion return to prepregnancy rates (2, 4, 10). For women who breast-feed, some studies have reported decreases in urinary calcium output during full lactation, suggestive of renal calcium conservation (4, 10–12), but not others (5, 13). Breast-feeding women also have reduced urinary phosphate excretion and elevated serum phosphate concentrations, indicative of renal phosphorus conservation (12, 14). Further decreases in calcium excretion have been reported after breast-feeding has stopped (5), but the data are inconsistent and some studies indicate that urinary calcium output increases toward nonpregnant, nonlactating

1 From the MRC Human Nutrition Research, Cambridge, United Kingdom, and MRC Keneba, The Gambia.
3 Address reprint requests to A Prentice, MRC Human Nutrition Research, Downham’s Lane, Milton Road, Cambridge, United Kingdom CB4 1XJ. E-mail: ann.prentice@mrc-hnr.cam.ac.uk.

rates during long lactation and after weaning (4, 14). Interpretation of these results may be complicated by alterations in maternal dietary calcium intake during and after lactation.

Biochemical markers of bone resorption and formation, including osteocalcin, are elevated in the first months of lactation (12, 14–16), but decrease after 6–12 mo, even in women who continue to breast-feed for ≥18 mo (14). Indications from longitudinal studies suggest that bone turnover is higher in the first months of lactation than at the end of pregnancy. There is evidence of an asynchrony in the patterns of change between bone resorption and formation in the postpartum period, with the peak resorption rate preceding the peak formation rate by several weeks (14). Duration of lactation influences the patterns of metabolic change, which are longer and more pronounced in those who breast-feed for longer periods (8, 15), but some changes are evident postpartum even in women who do not breast-feed (17).

It is not clear what hormonal mechanisms are responsible for these changes in calcium and bone metabolism. Elevated calcitonin concentrations in early lactation followed by a decrease to normal concentrations have been reported in some studies (14) but not others (4, 18). However, the other classic calcitropic hormones, parathyroid hormone and 1,25-dihydroxyvitamin D, are not elevated in lactation compared with concentrations measured before conception or in nonpregnant, nonlactating control women and are, if anything, slightly depressed (4, 5, 10, 14, 19, 20). Postpartum changes in the 3 calcitropic hormones are independent of whether and for how long a mother breast-feeds and do not correlate with bone turnover markers, breast-milk calcium, bone mineral status, or lactation-associated hormones such as parathyroid hormone–related protein and prolactin (14, 18, 20). During the weaning process—as the frequency of suckling declines, milk volume decreases, the estradiol concentration rises, and menses resume—there is an increase in calcium absorption (10, 21) that is accompanied by increases in parathyroid hormone and 1,25-dihydroxyvitamin D (5, 12), although this finding is not consistent among studies (22). Vitamin D status, as measured by circulating 25-hydroxyvitamin D (calcidiol) concentration, decreases in the months postpartum, at least in American mothers (18, 20), but this is independent of lactation. It is clear, therefore, that other hormonal mechanisms, as yet unidentified, must be involved in regulating the homeorhetic changes in calcium and bone metabolism associated with human pregnancy and lactation.

Interpretation of these patterns of change is complicated by the increases in extracellular volume and glomerular filtration rate that accompany pregnancy, and by altered tissue distributions resulting from the development of the fetal, placental, and mammary compartments. In addition, differences in the characteristics of groups of breast-feeding and control women and in the timing of measurements make direct comparisons between studies difficult. However, the patterns of change are consistent with the uptake and mobilization of calcium by the maternal skeleton to meet the high requirement for fetal growth toward the end of gestation and for breast-milk production during lactation, with subsequent restoration in the later stages of lactation and after weaning.

BONE MINERAL STATUS

The biochemical data suggest that human pregnancy and lactation are accompanied by the uptake and release of calcium from the skeleton during pregnancy and that mobilization of calcium continues, possibly at an increased rate, during the early months of lactation with a return to prepregnancy rates during or after weaning. This implies that changes must occur in the amount of bone mineral in the mother’s skeleton. If these changes are of sufficient magnitude to increase or decrease the mother’s bone mineral status in the long term, pregnancy and lactation could alter the woman’s risk of osteoporosis later in life. Retrospective studies of postmenopausal women investigating the possible effect on osteoporosis risk of having been pregnant or of having lactated produced conflicting results, possibly because of the difficulties of defining reproductive history adequately and of controlling for possible confounders such as socioeconomic factors and body size (23, 24).

Only in the past few years has the technology developed sufficiently for this possibility to be investigated directly in prospective studies. Absorptiometry, particularly dual-energy X-ray absorptiometry, is a technique that permits the measurement of whole-body and regional bone mineral content with such high precision and reproducibility that longitudinal studies of changes in bone mineral status within healthy individuals have become feasible (25). Several investigations by different research groups that have monitored postpartum bone changes in lactating and nonlactating mothers have been reported. In particular, data are becoming available from intensive studies in which women have been measured before conception and followed through and beyond pregnancy and lactation. Absorptiometric techniques, however, are not suitable for measurements during pregnancy, except for techniques that use instruments to measure the arms or legs, such as single-photon absorptiometry, and this limits the information that is currently available.

The overall picture emerging from these studies is that breast-feeding is accompanied by measurable reductions in maternal bone mineral content during the first 3–6 mo that are reversed during later lactation and after weaning (11, 12, 16, 17, 26–29). The reductions in bone mineral are most marked in the axial skeleton, where decreases at the spine and hip average ≈3–5%. Such rates of change are considerable and exceed those observed in women in the postmenopausal period (typically 1–3% per annum). The magnitude and duration of lactation-associated reductions in bone mineral are greater in women who breast-feed for a longer time (11, 26) and occur to a lesser extent, or are not seen at all, in mothers who do not breast-feed (17, 27, 29, 30). Breast-milk volume has been identified as a predictor of the magnitude of lactational bone mineral loss in the first 3 mo (30). There is, however, wide variability in the bone response to lactation even in women who are breast-feeding exclusively, such that decreases of nearly 10% at the spine have been reported in some individuals by 3 mo whereas no change is apparent in others (30). The magnitude of the bone response is not related to the initial bone mineral status of the mother or to her dietary calcium intake (30).

An increase in bone mineral content occurs in later lactation, even in mothers who continue to breast-feed and produce high volumes of milk into the second or third year after delivery (11, 27). For women who breast-feed for comparatively short periods, the reversal occurs after breast-feeding stops, and for those who conceive during lactation, the rise in bone mineral appears to occur during pregnancy (13). It is possible that the increase in bone mineral is associated with the increase in estrogen concentrations that herald the return of menstruation. For example, lactating women with an early return of menses have smaller bone loss during lactation and greater bone gain after weaning (29).
However, the close link between length of lactation and period of amenorrhea makes it difficult to examine their independent influence on bone mineral status and it is possible that neither factor is directly involved but gives information about some aspect of lactation behavior, such as sucking frequency or intensity (27).

The extent to which bone mineral status returns to “normal” after pregnancy and lactation is still uncertain. In a recent British study in which women were examined at 12 mo postpartum (or at 3 mo postlactation for women who breast-fed for > 9 mo), the bone mineral content of the whole body, trochanter, and lumbar spine was higher; that of the femoral neck and wrist was lower; and that of the radial shaft was not significantly different from that measured immediately postpartum (27). These changes were largely independent of whether the mother had breast-fed or not, and of how long breast-feeding had been continued (13). A similar pattern was observed in an American study except that women who breast-fed for > 6 mo had lower lumbar spine and femoral neck bone mineral at 12 mo than those who had breast-fed for a shorter period (26), possibly because insufficient time had elapsed for full recovery to have occurred in those women who were still lactating or had only recently stopped breast-feeding. In contrast, in an Italian study of women who breast-fed for 6 mo and then stopped, the bone mineral content of the lumbar spine and distal radius was lower 12 mo postpartum than immediately postpartum or when compared with a group of nonlactating control subjects postpartum (16).

To date, only 2 small longitudinal studies have compared a woman’s bone mineral status before conception with that measured after lactation or after resumption of menses (4, 5). Both suggest that bone mineral status may be reduced slightly as a result of pregnancy and lactation. However, these results are difficult to interpret because neither study included nonpregnant, nonlactating control subjects to monitor the reproducibility of the measurements or the influence of external factors such as seasonal change, and the final measurements were made close to or before the end of lactation, when changes in calcium and bone metabolism may still have been occurring.

Effects on bone mineral status during pregnancy itself are more difficult to determine because of the lack of suitable methods and the fact that the postpartum measurement may be influenced by lactation behavior. Three small studies that have measured a woman’s bone mineral status at a variety of skeletal sites before conception and after parturition produced conflicting results (4, 5, 28, 31). It may be that these studies were confounded by events that occurred before conception that may affect the way in which the maternal skeleton responds to pregnancy. Women who conceive during or shortly after breast-feeding for 6 mo, for example, show recovery of lactation-associated reductions in bone mineral content during the subsequent pregnancy whereas those who conceive at a later stage, once this recovery has occurred, show little overall change (13, 32).

**IMPORTANCE OF CALCIUM INTAKE**

Observational and supplementation studies suggest that the changes in calcium and bone metabolism that accompany lactation are independent of the current calcium intake of the mother (24, 30, 33). When correlations with calcium intake have been recorded (17, 34), they have been for overall status and not for the magnitude of change experienced during lactation, and likely reflect the interrelations between bone mineral density, body size, and dietary intake (35) rather than the fact that lactational bone response is modified by maternal calcium nutrition. Particularly compelling is the evidence from randomized, controlled trials of calcium supplementation that have shown no discernible effect of the intervention on lactation-associated changes in bone mineral content, breast-milk calcium concentration, fractional calcium absorption, or biochemical markers of bone turnover, even in women with very low calcium intakes (11, 14, 28, 36, 37). This is despite differences that have been identified between lactating women and control subjects in the acute response to an oral calcium load (38). Adolescent mothers may be an exception because a study in the United States indicated that lactation-associated bone changes were attenuated in girls consuming a high-calcium diet compared with those with lower intakes (39). However, no differences were observed between teenage and adult lactating Gambian women in their response to calcium supplements, despite their very low customary calcium intakes (11, 14).

The effect of calcium intake in pregnancy is less certain because there have been few studies of it. Pregnancy-associated alterations in calcium and bone metabolism, however, are evident even in women with very high calcium intakes, and calcium supplements appear to have little effect (5, 40). In addition, the changes in calcium absorption that occur during pregnancy suggest that the physiologic adjustments are likely to cover the increased requirements of the mother without a need for her to increase her calcium intake. However, there is some evidence that mothers with a customarily low calcium intake may benefit from higher calcium intakes during pregnancy. These include the observation that the bone mineral contents of neonates born to Indian women from poor social class backgrounds were higher if the mothers had received a calcium supplement during pregnancy (41), and that breast-milk calcium concentration, and hence the calcium intake of the breast-fed infant, may be influenced by maternal calcium intake during the preceding pregnancy (42). In addition, a low calcium intake is associated with an increased risk of pregnancy-induced hypertension and related obstetric complications, and calcium supplementation has been shown to reduce the blood pressure of pregnant women and their offspring in some studies (43; DA McCarron, unpublished observations, 1998). To what extent these effects indicate the correction of a nutritional deficit or the pharmacologic action of calcium independent of customary calcium intake is, as yet, unknown and needs further detailed research.

**IMPLICATIONS**

Recent studies have shown that lactation is associated with dramatic but temporary changes in bone mineral status and in calcium and bone metabolism, and that the pattern and magnitude of the response depends on the lactation behavior of the mother. However, despite wide variations between individual women, there is no evidence that these changes reflect insufficiencies in dietary calcium supply or that they can be prevented by an increase in calcium intake. The lactation-associated decreases in bone mineral status are reversible and by 3 mo postweaning there is little to distinguish mothers who have breast-fed from those who have not, including those who have breast-fed for an extended period.

Breast-feeding mothers transfer an average of ≈5 mmol (200 mg) Ca/d to their infants and this can exceed 10 mmol/d (400 mg/d) for some women (24). Because this is a substantial
proportion of the daily calcium intake of many mothers, there are widespread concerns that lactational performance may be impaired in women with a low calcium intake and that breast-feeding may have a deleterious effect on the long-term bone health of the mother. The available evidence suggests that such anxieties are unfounded and that considerations about the adequacy of an individual’s dietary calcium intake or her risk of postmenopausal osteoporosis should not influence her decision to breast-feed. As yet, the picture is less clear for pregnancy and more research is needed to determine the magnitude and limitations of the adaptive response before sound recommendations about appropriate calcium intakes can be made for pregnant women.

REFERENCES


