Postpartum Resolution of Hypocalcemia in a Lactating Hypoparathyroid Patient

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Abstract

A 24 year old woman with post-surgical hypoparathyroidism was studied during pregnancy and lactation. During pregnancy the patient required less vitamin D therapy for control of her hypoparathyroidism and, while lactating, maintained a normal serum calcium without any supplemental vitamin D. The serum parathyroid hormone concentration and plasma 1,25 (OH)₂ vitamin D concentration were undetectable and low normal respectively at a time when the serum calcium concentration was normal and the patient was not on vitamin D therapy. Urinary calcium excretion was low during this period and may explain the normalization of the serum calcium. The mechanism by which the improvement in calcium metabolism occurred is unknown, but may be secondary to a direct effect of prolactin on calcium homeostasis.

Significant alterations in calcium metabolism take place during both pregnancy and lactation (Heaney and Skillman, 1971; Pitkin, 1975). These alterations are thought to be related to dynamic changes in parathyroid hormone secretion and the synthesis of 1,25 (OH)₂ vitamin D in response to the maternal need for calcium in fetal skeletal development and for lactation (Pitkin, 1975; Toverud and Boass, 1979). The occurrence of pregnancy in a patient with hypoparathyroidism offers a unique opportunity to observe what adaptation may occur when the normal physiological responses to pregnancy are interrupted.

It has been reported that the symptoms of tetany are improved during both pregnancy (Aceto et al., 1966; Bronski et al., 1968; Grant, 1953) and lactation (Grant, 1953) in hypoparathyroid women. Wright et al. (1969) reported the development of post-partum hypercalcemia in two hypoparathyroid patients. Elevated to normal serum calcium concentrations were maintained on reduced to no vitamin D therapy for as long as three months post-partum.

We have recently had the opportunity to study a hypoparathyroid pregnant patient who exhibited a decrease in vitamin D requirement during pregnancy and lost all
requirement for vitamin D during lactation.

**Case Summary**

The patient is a 26 year old Caucasian female who had a total thyroidectomy in August 1970 for papillary adenocarcinoma of the thyroid followed by post-surgical hypoparathyroidism as evidenced by hypo-calcemic tetany and low levels of serum immunoreactive parathyroid hormone (<150 pg/ml) (Woo and Singer, 1974). She was treated with varying doses of vitamin D₂ or dihydrotachysterol and supplemental oral calcium and was found to be resistant to vitamin D therapy, requiring up to 300,000 units of vitamin D₂ and 3 grams of elemental calcium orally for marginal control of the hypocalcemia (serum calcium

![Graph of serum calcium, calcitriol, and plasma 1,25 (OH)₂ vitamin D concentrations during lactation and pregnancy.](image)

Fig. 1. Serum calcium concentration, plasma 1,25 (OH)₂ vitamin D concentration, and therapy with calcitriol. In early pregnancy the serum calcium and plasma 1,25 (OH)₂ vitamin D concentrations were low. Therapy with calcitriol 0.5 ug/day maintained the serum calcium concentration within the normal range. Treatment with calcitriol was discontinued immediately post-partum because of serum calcium concentration of 10 mg/dl. During lactation the mean serum calcium was 9.5 mg/dl while on no vitamin D treatment and during which time the plasma 1,25 (OH)₂ vitamin D concentration was low normal. Following cessation of lactation the serum calcium fell to 7.5 mg/dl and the patient became resistant to the effect of calcitriol.
During 1977 the patient became pregnant and was referred to the Los Angeles County/University of Southern California Medical Center in her second month of pregnancy. She was taking dihydrotachysterol, 1.0 mg per day at that time and the average serum calcium was 7.0 mg/dl. The serum albumin concentration was 4.1 gm/dl and remained normal throughout the study period (4.1 ± 0.2 gm/dl, mean ± SD). It was elected to place the patient on therapy with 1,25 (OH)2 vitamin D3 (calcitriol) for closer control of the serum calcium during the pregnancy. A dose of 0.5 ug of calcitriol per day maintained the serum calcium at an average concentration of 8.5 mg/dl (Figure 1) and the patient was free of any symptoms of tetany.

On August 21, 1978, the patient gave birth to a normal 8 lb. 6 oz. baby boy and then began breast feeding. The serum calcium rose to 10.0 mg/dl the second postpartum day and therapy with calcitriol was stopped. The patient continued to breast feed for four months. During this time the mean serum calcium was 9.5 mg/dl while on no vitamin D therapy. As shown in Figure 1, the plasma concentration of 1,25 (OH)2 vitamin D (Chandler et al., 1980) was low normal both prior to calcitriol therapy and during lactation (normal=20–45 pg/ml). An oral calcium tolerance test (Broadus et al., 1980) was performed while the patient was breast feeding and on no vitamin D therapy (Table 1). The serum calcium and serum phosphate concentrations were high normal (10.1 mg/dl and 4.2 mg/dl respectively) prior to the ingestion of 1 gram of calcium. The serum calcium rose only to 10.3 mg/dl post-calcium ingestion. Nephrogenous cyclic AMP excretion was low (0.37 nmol/100 ml GF) and the renal phosphate threshold (TmPO4) was high (5.4 mg/100 ml GF), suggesting absent or suppressed parathyroid hormone effect. Despite this, urinary calcium excretion was very low (0.024 mg/100 ml GF) relative to the high filtered calcium load and the hypoparathyroid state. Serum prolactin concentration increased with suckling as shown in Figure 2.

The patient stopped breast feeding after four months. One week later she began to have muscle cramps and tetany. As demonstrated in Figure 1, the serum calcium concentration had fallen to 7.5 mg/dl. Therapy with calcitriol was re instituted. Over the ensuing 6 months the dose was raised to as high as 2.5 ug per day of calcitriol during which time the peak in the serum calcium concentration was 7.6 mg/dl. Currently the patient remains resistant to

<table>
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<tr>
<th>Serum Ca</th>
<th>Serum Albumin</th>
<th>Serum PO4</th>
<th>Urine Ca</th>
<th>TmPO4*</th>
<th>Nephrogenous cAMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/dl</td>
<td>gm/dl</td>
<td>mg/dl</td>
<td>mg/100 ml GF</td>
<td>mg/100 ml</td>
<td>nmol/100 ml GF</td>
</tr>
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<td>3.9–5.0</td>
<td>2.5–4.2</td>
<td>.03–0.13</td>
<td>2.5–4.2</td>
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<tr>
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<td>10.1</td>
<td>4.1</td>
<td>4.2</td>
<td>0.024</td>
<td>5.4</td>
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<tr>
<td>Post-Ca Ingestion</td>
<td>10.3</td>
<td>4.1</td>
<td>4.8</td>
<td>0.026</td>
<td>4.4</td>
</tr>
</tbody>
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* TmPO4 = renal phosphate threshold
therapy. Dihydrotachysterol, 3.0 mg per ration at 8.0 mg/dl.

day, maintains the serum calcium concent-

Comments

The onset of pregnancy in this patient with post-surgical hypoparathyroidism was marked by a decreased resistance to vitamin D therapy which was present prior to the pregnancy and following lactation. Optimal control of the serum calcium concentration was achieved with 0.5 ug of calcitriol per day during the pregnancy whereas control was inadequate with as much as 2.5 ug per day of calcitriol following cessation of breast feeding. Even more remarkable was the observation that the serum calcium concentration remained normal during lactation while the patient was on no vitamin D therapy. Discontinuation of breast feeding resulted in a rapid fall in the serum calcium, symptoms of tetany, and return of resistance to vitamin D therapy.

During normal pregnancy the increased demand for calcium for fetal development and for lactation in the post-partum period is thought to be achieved in a number of ways. Some studies have shown an increase in serum immunoreactive parathyroid hormone concentration (IPTH) which is most apparent in the last trimester of pregnancy (Cushard et al., 1972; Reitz et al., 1977;
Drake et al., 1979; Pitkin et al., 1979; Conforti et al., 1980) and during lactation (Retallack et al., 1977). This is not a consistent finding as several studies have not found an increase in IPTH during pregnancy (Hillman et al., 1978; Wieland et al., 1980; Whitehead et al., 1981). An increase in PTH secretion could be responsible for an increase in the synthesis of 1,25 (OH)₂ vitamin D although the increase in the plasma concentration of 1,25 (OH)₂ vitamin D during pregnancy and lactation appear to precede the rise in the plasma concentration of IPTH (Cushard et al., 1972; Reitz et al., 1977; Drake et al., 1979; Pitkin et al., 1979; Conforti et al., 1980; Retallack et al., 1977; Kumar et al., 1979; Fleischman et al., 1980; Gertner et al., 1980; Steichen et al., 1980; Whitehead et al., 1981). This could in turn explain the enhanced intestinal calcium absorption observed during pregnancy (Heaney and Skillman, 1971; Pitkin, 1975; Toverud and Boass, 1979). Fractional intestinal calcium absorption has been found to be increased in vitamin D deficient parathyroidectomized lactating rats (Boass et al., 1981) suggesting the presence of a modulator of intestinal calcium absorption other than 1,25 (OH)₂ vitamin D. Urinary calcium excretion is decreased during late pregnancy and lactation (Goss, 1962; Heaney and Skillman, 1971; Toverud and Boass, 1979) and may also be the result of an increase in PTH secretion (Cushard et al., 1972; Reitz et al., 1977; Drake et al., 1979; Pitkin et al., 1979; Conforti et al., 1980). Serum calcitonin concentrations have been reported to be high in pregnancy in some women (Samaan et al., 1975; Drake et al., 1979; Pitkin et al., 1979; Stevenson et al., 1979; Conforti et al., 1980; Kovanick et al., 1980; Whitehead et al., 1981) and may serve to protect against the skeletal resorptive effects of PTH and 1,25 (OH)₂ vitamin D (Stevenson et al., 1979). When dietary calcium deficiency is present during pregnancy and lactation in rats, however, a marked loss of mineral from bone occurs (Toverud and Boass, 1979) and the skeleton thereby may serve as a maternal source for the fetal calcium need.

The mechanism responsible for the decreased vitamin D requirement in our patient is unknown. The high TmPO₄ and low nephrogenous cyclic AMP excretion indicate an absent or suppressed parathyroid hormone effect and correlate well with the undetectable level of IPTH in the serum. The low urinary calcium excretion observed in our patient during lactation was most unusual in a hypoparathyroid patient with a serum calcium concentration of 10.1 mg/dl. This observation could account for the return to normal of the serum calcium concentration during lactation. The low normal plasma 1,25 (OH)₂ vitamin D concentration and the lack of a significant calcemic and hypercalciuric response following the oral calcium tolerance test during breast feeding suggest that 1,25 (OH)₂ vitamin D and intestinal calcium absorption did not play a major role in the normalization of the serum calcium. Since an increase in bone resorption can be seen in pregnancy and lactation (Toverud and Boass, 1979) it is possible that an increased flux of calcium out of the skeleton in this thyroidectomized, presumably calcitonin deficient patient, may have played a role in the normalization of the serum calcium concentration. It is unlikely that sex steroids played a direct role in decreasing the vitamin D resistance since estrogen antagonizes the effect of PTH on bone in vitro (Stern, 1969) and may actually induce tetany in hypoparathyroidism (Burckhardt et al., 1975).

It seems apparent that neither PTH nor 1,25 (OH)₂ vitamin D was responsible for the improvement in calcium metabolism in our patient. Prolactin has been suggested to enhance intestinal calcium absorption in pregnancy and lactation, possibly through a direct stimulating effect on renal 25-
hydroxycholecalciferol-1-hydroxylase activity and consequent increased formation of 1,25 (OH)₂ vitamin D (Spanos et al., 1976). However, the concentration of 1,25 (OH)₂ vitamin D in hyperprolactinemic patients is normal (Adams et al., 1979; Kumar et al., 1980). While prolactin was increased in our patient, the serum 1,25 (OH)₂ vitamin D level remained low normal. Recent experiments in vitamin D-deficient rats suggest that prolactin may directly increase intestinal calcium transport and bone calcium mobilization (Pahuja et al., 1981). It is also possible that prolactin may increase the serum calcium concentration by increasing fractional renal calcium reabsorption. While prolactin may be responsible for the normalization of the serum calcium in our patient, an effect of a metabolite of vitamin D other than 1,25 (OH)₂ vitamin D or another unknown factor cannot be excluded.

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References


