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Features of bone metabolism during lactation

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Abstract: The mineralization of the skeleton of a child during the period of exclusive breastfeeding occurs only at the expense of the mother's body. The main mechanism for providing the necessary calcium content in breast milk is the temporary demineralization of the mother's skeleton. The concentration of calcium in milk reaches a maximum during the first 3 months after birth and then decreases, however, in the next 3–4 months, the volume of lactation increases as much as possible, and therefore excretion calcium remains approximately at the same level until the introduction of complementary foods. Bone mineral density in the first 6 months of lactation decreases by 1–3% per month, reaching 3–10% in six months. The rate of calcium release from the bone tissue of a nursing woman depends solely on the intensity of lactation, other factors, in particular, the content of calcium, vitamin D and other elements in the diet, have practically no effect on it. In a classic study by Donelson et al. it was possible to find out that a negative calcium balance is formed in the body of a nursing woman, which cannot be prevented by additional intake of calcium, phosphorus and vitamin D.

Keywords: bone density, resorption, remineralization, phosphatase, tubular and spongy bones

Purpose of the study: To find scientific data and identify characteristic changes in bone metabolism during lactation.

Materials and Methods: Articles, technical books, and consistent publications from national and international organizations were searched. The following keywords were used: "bone metabolism in women" lactation period "," remineralization and demineralization "and" breastfeeding ". References cited in selected articles have also been included.

Metabolic processes in bone tissue during lactation

The metabolic processes in bone tissue during lactation are very intense. The levels of bone resorption markers in the postpartum period increase by 2–3 times compared with the last trimester of pregnancy. Serum levels of markers of bone synthesis after childbirth are also elevated, although to a lesser extent. The level of alkaline phosphatase decreases immediately after delivery (mainly due to the placental fraction), but remains high also due to the bone fraction. Consequently, the biochemical parameters characterizing the processes of metabolism in the bone tissue indicate the predominance of the processes of its resorption [1].

A decrease in bone mineral density during lactation has also been confirmed in a number of studies in which this indicator was determined directly by densitometry. Small prospective studies have documented a 3–10% decrease in postpartum bone mineral density in breastfeeding women between 2 and 6 months postpartum [2]. Demineralization processes occur most intensively in spongy bones: lumbar vertebrae, in certain areas of the femur, distal radius, and much less in tubular bones. The decrease in bone mineral density during lactation occurs very intensively - 1-3%

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per month, which is quite a lot when compared with the loss of mineral density in postmenopausal women (1-3% per year). The microarchitectonics of bones changes: trabeculae become thinner, perforations appear in them. As the intensity of lactation decreases, these changes quickly regress [3].

Starting from the second half of the year after the birth of a child - from the moment non-dairy food is introduced into the baby's diet - demineralization of bone tissue stops, despite the fact that lactation continues. Bone mineral density gradually increases, reaching normal levels about 12 months after birth. Restoration of the calcium content in the bones occurs regardless of whether the mother continues to breastfeed or not, while in the case of continued lactation, remineralization occurs somewhat more slowly [4]. The degree of mineralization increases by 0.5–2% per month, which significantly exceeds the rate typical for the treatment of osteoporosis. Restoration of bone mineral density occurs unevenly; The tubular bones remineralize the fastest, while the density of cancellous bones, in particular the lumbar vertebrae, remains low the longest [5].

Remineralization and demineralization of bones during lactation

The mechanisms that promote active bone remineralization and are activated from the moment the volume of lactation decreases have already been partly mentioned earlier. First of all, with a decrease in the volume of lactation, calcium excretion with milk decreases (at the maximum volume of lactation (1 liter/day), about 200 mg of calcium is excreted from the mother's body) [6].

At the same time, calcium absorption from the mother's alimentary canal is enhanced.

In rare cases during lactation, more pronounced than normal demineralization of skeleton occurs. It is believed that it is caused by an increased level of PTHrP due to hypersecretion of this peptide in the mammary glands during their hyperplasia, although these changes completely regress after the end of lactation [9]. Another cause of lactation-associated osteopenia may be, as in the case of osteopenia during pregnancy, low bone mineral density even before conception [10].

Features of the regulation of mineral metabolism during lactation

During lactation, PTH-like peptide regulates calcium resorption from the maternal skeleton, calcium reabsorption in the renal tubules, and correlates negatively with serum PTH and positively with ionized calcium [11].

Increased calcium reabsorption by the kidneys persists throughout the entire period of complementary feeding and for some time after the complete cessation of lactation [7].

Experimental studies have shown that a possible mechanism for intensive restoration of bone density is the rapid apoptosis of osteoclasts immediately after the cessation of lactation and a significant increase in the number of osteoblasts formed from progenitor cells that multiply rapidly [8].

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During lactation, PTH-like peptide regulates calcium resorption from the maternal skeleton, calcium reabsorption in the renal tubules, and correlates negatively with serum PTH and positively with ionized calcium [11].

A special role in the regulation of calcium-phosphorus metabolism belongs to vitamin D. Vitamin D is a hormone of secosterol, which is present in the human body in endogenous (vitamin D3) and exogenous (vitamin D2) forms. The endogenous form of vitamin D, cholecalciferol (vitamin D3), is synthesized in the skin from the cholesterol metabolite 7-dehydrocholesterol under the influence of ultraviolet radiation. Vitamin D3 is also available in oral supplements. The exogenous form of vitamin D (vitamin D2) (ergocalciferol) is produced by ultraviolet irradiation of the plant styrene ergosterol and is available from plant foods. Both forms of vitamin D undergo further metabolism. Vitamin D metabolites circulate in the blood via specific vitamin D binding proteins. Vitamin D3 and vitamin D2 are present in humans in a ratio of approximately 2:1. In the kidney, vitamin D is also converted to 24-hydroxylated metabolites, which are generally inactive but may have unique effects on chondrogenesis and intramembranous ossification. Many of the effects of vitamin D metabolites are mediated by nuclear receptors or by effects on target cell membranes. In the liver, vitamin D is converted by hydroxylase to 25-hydroxyvitamin D, the main form of vitamin D [12]. Thus, serum 1,25-dihydroxyvitamin D levels are the best indicator of overall vitamin D status. In the proximal tubule of the kidney, 25-hydroxyvitamin D is hydroxylated to form 1,25-dihydroxyvitamin D, the most active form of the hormone. The animal form is represented by 1,25-dihydroxycholecalciferol [1,25(OH)2D3]. This hydroxylation step is activated by several factors, the most important of which are PTH and low concentrations of calcium, phosphorus, and 1,25-dihydroxyvitamin D itself. The 1-alpha-hydroxylase that mediates this conversion in the kidney is also produced in the placenta and keratinocytes. The normal serum concentration of 1,25-dihydroxyvitamin D is about 20–60 pg/mL. The kidney can also convert 25-hydroxyvitamin D to 24,25-dihydroxyvitamin D. The content of this metabolite is 100 times greater than that of 1,25-dihydroxyvitamin D, but its biological role is unclear. Some researchers suggest that this breakdown product does not have any important biological effects, others believe that it is involved in chondrogenesis and bone formation, especially intramembranous structures. Vitamin D and its metabolites are inactivated in the liver by conjugation with glucuronides or sulfates and oxidation of their side chains. Mutations in the 24-hydroxylate enzyme have recently been shown to cause hypercalcemia and hypercalciuria in children and adults [13]. In this state, the level of 1,25-dihydroxyvitamin D is elevated due to insufficient metabolism of 1,25(OH)2D [13]. The biological effects of vitamin D and its mechanism of action are as follows. Vitamin D mediates its biological effects through the nuclear hormone receptor, the vitamin D receptor (VDR) [14]. The receptor binds many vitamin D metabolites, which reflects their biological effects, and therefore

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1,25-dihydroxyvitamin D has the highest affinity for the receptor. VDR regulates gene transcription by homodimerization and heterodimerization with the retinoic acid receptor. The complex binds to target DNA sequences and regulates the transcription of several genes important in directing vitamin D to calcium and skeletal metabolism and its various biological effects. Vitamin D metabolites, as well as other steroid hormones, can act through the membrane receptor to cause rapid changes in calcium flux in the cell. Vitamin D increases intestinal calcium absorption, primarily in the jejunum and ileum, by increasing calcium absorption across the enterocyte boundary membrane. To do this, vitamin D induces calcium-binding calbindins, which are involved in the transport of calcium through the cell, and through its action on the membrane structures that transport calcium; it promotes the outflow of calcium from the basolateral side of the enterocyte. Initially, the effect of vitamin D on intestinal calcium absorption lasts for several minutes, so the effect of vitamin D on intestinal calcium transport may also be mediated by a membrane non-genomic receptor. As a result, the efficiency of intestinal transport of calcium is increased. In vitamin D deficiency, only 10–15% of dietary calcium is absorbed by the gastrointestinal tract, but with sufficient vitamin D, about 30% of dietary calcium is absorbed. During pregnancy and lactation, elevated circulating concentrations of 1,25-dihydroxyvitamin improve intestinal absorption of calcium by 50–80%. Vitamin D also regulates skeletal metabolism via the RANK pathway, and 1,25-dihydroxyvitamin D also increases the efficiency of dietary phosphorus absorption by about 15–20%. Conclusions: Therefore, moderate bone demineralization during lactation is not a disease, but only a reliable mechanism for ensuring sufficient calcium in breast milk. This process is completely reversible, does not pose a danger to the mother's body and is fully compensated for up to about a year after the birth of the child, even if the mother continues to breastfeed.

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