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Changes in serum hydroxyvitamin D levels of breast cancer patients during tamoxifen treatment or chemotherapy in premenopausal breast cancer patients ☆

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Abstract ***Background:*** We investigated the effect of breast cancer adjuvant treatment on vitamin D status, as measured by serum hydroxyvitamin D (25OHD).
Methods: Premenopausal patients ($n = 483$) diagnosed with non-metastatic breast cancer in 2009 at Asan Medical Center had serum 25OHD levels prospectively analysed at diagnosis and 6 and 12 months after surgery. We excluded patients who took vitamin D supplements or received neoadjuvant chemotherapy. Vitamin D sufficiency was defined as a serum level of $\geqslant$30 ng/ml, insufficiency as 20–29 ng/ml and deficiency as <20 ng/ml.
Results: Compared with baseline serum 25OHD, patients who received chemotherapy had decreased serum 25OHD levels at 6 months (–5.52 ng/ml, $p = 0.003$) and 12 months (–1.24 ng/ml, $p = 0.517$) and patients who received anti-hormone therapy had significantly increased serum 25OHD levels at 6 months (+3.00 ng/ml, $p = 0.681$) and 12 months (+6.47 ng/ml, $p = 0.002$, respectively). Among patients who received chemotherapy, 49.5% were vitamin D sufficient at diagnosis but only 26.9% were sufficient 6 months after finishing chemotherapy and this percentage increased to 45.2% at 12 months.

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Conclusions: Vitamin D levels decrease during chemotherapy but recover after treatment ends. Anti-hormone therapy with tamoxifen causes serum vitamin D levels to increase. Whether the increased serum vitamin D affects the antitumour effect of the tamoxifen has yet to be determined.

1. Introduction

The study of vitamins has extended beyond bone health and calcium metabolism [1]. Evidence for an association of vitamin D with breast cancer has been obtained from epidemiological studies that found that higher cancer rates in northern latitudes were related to vitamin D deficiency [2]. However, observational studies examining the association between vitamin D intake or blood levels and cancer risk in general, and breast cancer risk in particular, have yielded inconsistent results [3–5]. An inverse association between serum hydroxyvitamin D (25OHD) levels and risk of breast cancer recurrence and mortality in women diagnosed with breast cancer has been observed in recent prospective studies [6,7]. Vitamin D is also important for bone, neuromuscular and cardiovascular health, as well as autoimmunity and infection. Bone health is a particular concern for survivors of breast cancer because breast cancer treatment induces early menopause in pre- and peri-menopausal patients, and aromatase inhibitors (AIs) cause bone loss in postmenopausal patients. Therefore, it is important for the overall health of breast cancer patients to maintain an optimal level of vitamin D.

Crew et al. reported that 400 IU daily of vitamin D did not change the vitamin D status of patients during chemotherapy [8]. There is disagreement regarding the effective vitamin D dose for obtaining anti-cancer effects, but it has been proposed that vitamin D deficiency should be treated with increasingly high doses of vitamin D [9]. A recent meta-analysis of nine studies of vitamin D supplementation showed that vitamin D supplementation in doses that ranged from 300 to 2000 IU/day was associated with a modest but significant reduction in mortality, and provides support for this hypothesis [5]. Vitamin D intoxication is extremely rare but is caused by more than 50,000 IU/day, which raises 25OHD levels to more than 150 ng/ml and is associated with hypercalcaemia and hyperphosphatemia [10].

Risk factors for vitamin D deficiency include increased age, darker skin pigmentation, obesity, low dietary intake and sun avoidance behaviours. Korea lies between latitudes 33 and 43 degrees north and is thus considered to have abundant sunlight. However, because of this, nutritional vitamin D status has not been much discussed and the possibility of obtaining additional supplies of vitamin D from the diet has also been neglected [11]. Moreover, Asian women, including Korean women, and especially older women, are reluctant to be exposed to sunlight. As a result, vitamin D deficiency is prevalent in the general population [12].

Most authorities suggest that a measurable blood level of 25OHD is required for vitamin D sufficiency. Circulating 25OHD levels provide an integrated measure of vitamin D from all sources and are considered the best indicator of vitamin D levels in body stores [13]. One recent review suggests that there may be an advantageous range of 25OHD levels that starts at 75 nmol/L (or 30 ng/ml) [14].

This study was undertaken to determine the prevalence of vitamin D deficiency at diagnosis and during and after adjuvant treatment in breast cancer patients.

2. Patients and methods

The study was approved by the institutional review board of Asan Medical Center.

2.1. Study population

Patients were drawn from the Asan Medical Center Breast Cancer Database, a prospectively maintained web-based system that includes information on all patients who have had breast cancer operations at Asan Medical Center. The database provides detailed information on breast tumour type, and date of breast cancer recurrence. We retrospectively analysed the data of 1036 premenopausal breast cancer patients diagnosed in 2009 whose serum 25OHD levels were checked every 6 months. Exclusion criteria included receipt of neoadjuvant chemotherapy, metastatic breast cancer and prior vitamin D supplementation. Patients who did not have serum vitamin D examinations every 6 months, or who took vitamin D supplements during the follow-up period were excluded from the final analysis Therefore, a total of 483 patients were analysed in this study, of which 68 patients had DCIS breast cancer. The patients received chemotherapy, anti-hormone therapy or radiotherapy according to standard treatment regimens. Those undergoing chemotherapy took dexamethasone as antiemetic for 2–3 days. For classifying body weights we use the World Health Organisation (WHO) classification which regards a BMI of less than 18.5 as underweight, while a BMI of over 25 is considered overweight. We measured serum 25OHD levels before surgery, as well as 6 and 12 months after surgery (Fig 1).