Discussion regarding vitamin D deficiency in patients at the Lynchburg Hematology-Oncology Clinic began after a nurse practitioner attended a meeting of the Virginia Council of Nurse Practitioners in March 2006. The topic of bone health was presented, and vitamin D deficiency was discussed as a contributing factor to decreased bone density. Appropriate laboratory testing and interpretation for deficiency were taught, as well as treatment strategies for various levels of insufficiency or deficiency.

The oncology clinic was aware of the potential side effect of decreased bone mineral density from aromatase inhibitors frequently used in treatment of hormone receptor-positive breast cancer (Lonning et al., 2005). Therefore, making appropriate hormonal therapy selections based on patients' histories related to bone health was routinely considered. When using aromatase inhibitors, patients are monitored for decreased bone density with a dual energy x-ray absorptiometry scan every two years and encouraged to take calcium supplements and participate in weight-bearing exercises.

In an effort to further promote the bone health of patients, the clinic began checking vitamin D levels in at-risk patients and recommended supplementation when appropriate.

Not long after the routine evaluation of vitamin D levels began in the clinic, a study reported that women on aromatase inhibitors with low vitamin D levels were more susceptible to worsening bone density than those with normal levels (Lonning et al., 2006).

Vitamin D Levels

Vitamin D receptors are found in more than 30 different tissues in the body. A normal vitamin D level is believed to be necessary for optimal functioning of these cells (“Snapshots,” 2006). The laboratory used by the clinic reports a normal vitamin D range between 32–100 ng/ml (other laboratories may report different normal ranges). Vitamin D deficiency is defined as a level less than 10 ng/ml and insufficiency is defined as a level from 10.1–31.9 ng/ml. Vitamin D level is evaluated with the 25-hydroxy vitamin D laboratory test. After testing symptomatic patients in the clinic, a majority had some level of insufficiency and some were severely vitamin D deficient (see Figure 1).

The results of patients whose vitamin D levels were checked from May–September 2006 were analyzed. The numbers of patients tested for the first time from May–September were 86, 89, 72, 59, and 81, respectively. Of those tested, most had a level below 30 ng/ml (75.4%, 84.1%, 66.6%, 69.3%, and 63%, respectively). The most common symptoms seen in the clinic and used to support vitamin D reimbursement are bone and muscle pain, fatigue, and hypocalcemia.

As the nurse practitioner became more aware of the number of patients in the clinic with low vitamin D levels, she began to research the subject more thoroughly. Was treating patients to get them to the low end of normal enough to promote optimal health? Some orthopedic and nutritional therapy researchers have recommended that vitamin D levels should be in the 40–50 ng/ml range to promote optimal health (Bischoff-Ferrari, Giovannucci, Willett, Dietrich & Dawson-Hughes, 2006; Holick, 2006; Vieth, 2006). It became clear in looking at the data collected that, if
50 ng/ml was used as a minimum for treatment in the clinic, more than 90% of the tested patients would need supplementation with vitamin D.

Supplements

When the clinic first began treating patients with vitamin D deficiency, it targeted those with levels below 30 ng/ml. Ergocalciferol and/or cholecalciferol was given weekly with dose and schedule based on the patient’s 25-hydroxy vitamin D level. The vitamin D supplements were given with other multivitamins or calcium supplements that patients already were taking. After following that treatment plan for a number of months, many patients continued to have low levels of vitamin D; some levels actually declined. Upon noting that trend, the nurse practitioner stopped cholecalciferol use and increased the frequency of ergocalciferol dosing. Ergocalciferol then was used on a weekly schedule until history showed that patients with the lowest vitamin D levels did not reach normal, even after 8–12 weeks of treatment.

Ergocalciferol dosing varies depending on the severity of the deficiency, but a 50 ng/ml level is the current minimum recommended goal of treatment. For example, a patient with a vitamin D level less than 10 ng/ml would be started on 50,000 IU orally once a day for seven days, then continue on 50,000 IU one to three times per week until reaching a level of 50–75 ng/ml. The patient then is put on maintenance therapy of 50,000 IU once or twice monthly, or more often if needed, to maintain those levels. Vitamin D and calcium levels are checked about 8–12 weeks after initiation of treatment and repeated at a similar interval until the patient begins maintenance therapy. At that point, the patient is monitored every three to six months. Less frequent dosing may be used with frail and older adults.

The maintenance dose of 50,000 IU monthly is roughly equivalent to 1,666 IU per day. This is given in addition to other supplements that the patient is taking, such as multivitamins or calcium supplements, that also have small amounts of vitamin D.

Natural Sources

Patients often ask about nutritional sources of vitamin D. The substance with the highest concentration of vitamin D is cod liver oil at 1,360 IU per tablespoon. Fish such as mackerel, tuna, and salmon (canned in oil) also are sources of vitamin D. Vitamin D fortified milk has 98 IU per 8 oz. serving (“Snapshots,” 2006).

Another source of vitamin D is skin exposure to sunlight. Short intervals of exposure (i.e., 10–15 minutes) have been shown to generate as much as 20,000 IU of vitamin D (Boyles, 2003). Patients are encouraged to use limited exposure to sunlight as a source of vitamin D; however, the latitude in some regions and the skin’s inability to convert vitamin D into a usable form may influence adequate absorption. Older adult patients’ skin is less likely to adequately absorb or convert enough vitamin D to support a normal level.

Toxicity Warning

Careful evaluation for toxicity is recommended for people on vitamin D supplementation. Toxicity has been shown in patients taking 10,000–40,000 IU or more per day and may include symptoms of nausea, loss of appetite, constipation, and behavioral changes most likely from hypercalcemia (Bischoff-Ferrari et al., 2006; Dranov, 2006; Vieth, 2006). Supplementation use in patients with a tendency for hypercalcemia or kidney stones may require more frequent monitoring or avoidance of this type of therapy.

Very few patients treated in the clinic have had significant side effects requiring the need for discontinuation of therapy. Three patients complained of significant diarrhea, although this was unexplained based on known side effects. A few patients complained of constipation to the degree that they chose to stop the treatment, but others were managed with dose adjustments. Several patients had vitamin D levels of more than 100 ng/ml but, after the initial
Several in vitro studies have shown that breast, colon, and prostate cancer cells, as well as osteosarcomas and melanomas, are responsive to the antiproliferative effects of vitamin D. to vitamin D therapy; however, two cases of nephrolithiasis have occurred in the clinic. Several patients complained of severe dizziness and weakness associated with treatment, even with levels less than 100 ng/ml, but they improved when therapy was discontinued.

Vitamin D supplementation at the clinic has evolved as resistance to therapy has been observed in a growing number of treated patients. Data comparing the treatment of the general population in central Virginia have not been evaluated, but anecdotal observations from a local orthopedic office reveal that patients require less vitamin D supplementation to reach normal levels than patients in the oncology clinic.

In addition, in a literature review, vitamin D supplementation may be supported as an adjunct to cancer treatments. Several in vitro studies have shown that breast, colon, and prostate cancer cells, as well as osteosarcomas and melanomas, are responsive to the antiproliferative effects of vitamin D (Holick, 2006). Multiple cancer prevention and treatment clinical trials with vitamin D therapy are ongoing.

Researchers have found that vitamin D insufficiency may weaken the immune system and make patients susceptible to diseases such as cancer. In 1980, a landmark article was published that showed a higher incidence of colon cancer in areas of the United States that receive less sunshine (Garland & Garland, 1980). A more recent article emphasized the increased incidence of ovarian cancer in women living in areas with lower sunlight exposure (“Snapshot,” 2006). In an analysis of vitamin D levels in patients with breast cancer, those with lower levels had a higher incidence of breast cancer and were more likely to have an advanced form of the disease (Garland et al., 2007). Another study stated that raising the vitamin D level to 34 ng/ml would reduce the incidence of colon cancer by half and projected a 66% reduction with serum levels of 46 mg/ml (Gorham et al., 2007). Vitamin D also may be associated with improved survival of patients with early-stage non-small cell lung cancer (Zhou et al., 2007). The need for further research in vitamin D therapy for patients with cancer was recently discussed at a National Cancer Institute Workshop (Davis, 2007).

Conclusion

The full impact of treating low vitamin D levels in the hematology/oncology population is unknown. Outcome information has not been collected in this clinic, but some comments from patients have described increased energy, reduced fatigue, less pain, reduced requirements for analgesics and, as one patient stated, “I feel normal again.” Oncology clinicians must be aware of the potential negative effects of low vitamin D levels in their patient populations and should consider testing for and treating this deficiency or insufficiency in their practices.

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