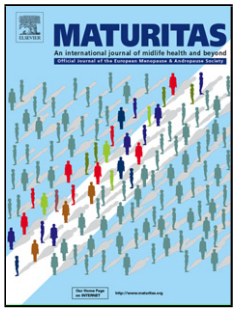

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National Osteoporosis Society Practical Clinical Guideline on Vitamin D and Bone Health

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11.

Introduction

There is growing interest in the importance of vitamin D in the maintenance of bone health and the prevention of falls and fractures. Although there is no universal consensus on the criteria for vitamin D deficiency, this is common in the UK, particularly in frail older people (1). This has resulted in a marked increase in requests for serum 25 hydroxyvitamin D (25OHD) estimation, but there has been confusion about the indications for these measurements, interpretation of the results and the management of vitamin D deficiency. The National Osteoporosis Society (NOS) has therefore developed a practical clinical guideline on the management of vitamin D deficiency in adults who have or may be at risk of developing bone disease (2). A summary of the guideline has also been published (3). The guideline was written by a group of clinicians and scientists with expertise in vitamin D and osteoporosis. It was based on evidence from the Institute of Medicine (IOM) report in 2010 (4), supplemented by literature reviews to identify papers published subsequently. In areas where evidence was unavailable, the Writing Group gave pragmatic advice, based on their own views and experience.

Assessment of Vitamin D Status

Measurement of serum 25OHD was considered to be the best way of estimating vitamin D status. Ideally, the assay used should have the ability to measure $25OHD_2$ and $25OHD_3$ equally. In practice, this means that it should use either high performance liquid chromatography or tandem mass spectrometry. Although some laboratories restrict 25OHD measurements to patients with an abnormal adjusted serum calcium, parathyroid hormone (PTH) or alkaline phosphatase, these changes occur late in the development of vitamin D deficiency (5), so where there are clinical grounds for suspecting vitamin D deficiency, 25OHD should be measured without the need for any preliminary investigations.

Indications for Serum 25OHD Measurement

The NOS guideline recommends that serum 25OHD measurements are considered in patients with bone diseases that may be improved with vitamin D treatment or where correcting vitamin D deficiency prior to specific treatment would be appropriate This group includes patients with vitamin D deficiency osteomalacia, where vitamin D treatment improves symptoms such as musculoskeletal pain, hyperalgesia, muscle weakness and a waddling gait. Correcting vitamin D deficiency is also likely to be beneficial in osteoporosis, but particularly in patients starting treatment with a potent antiresorptive agent such as zoledronate or denosumab, to avoid the development of hypocalcaemia. There are other bone diseases where correcting vitamin D deficiency before drug treatment is recommended, such as when treating Paget's disease with a bisphosphonate. Nevertheless, routine 25OHD testing is unnecessary in patients with osteoporosis or fragility fracture, where a decision has already been made to co-prescribe vitamin D supplementation with an oral antiresorptive treatment. Symptoms that may be due to vitamin D deficiency are often vague and it can be difficult to determine if they are due to a low serum 25OHD level. Nevertheless, serum 25OHD should be considered if patients are suspected of having symptoms caused by osteomalacia. Serum 25OHD measurements are not recommended in asymptomatic healthy individuals with no evidence of bone disease.

Interpretation of Serum 25OHD Measurements

The NOS guideline recommended the adoption of the following vitamin D thresholds advocated by the IOM (4):

- Serum 25OHD < 30 nmol/L is deficient
- Serum 25OHD of 30–50 nmol/L may be inadequate in some people
- Serum 25OHD > 50 nmol/L is sufficient for almost the whole population

Applying these criteria in clinical practice, vitamin D treatment is recommended when the serum 25OHD is less than 30 nmol/L. In patients with a serum 25OHD between 30–50 nmol/L, treatment is advised in the following situations:

- Fragility fracture
- Documented osteoporosis
- High fracture risk
- Treatment with antiresorptive medication for bone disease
- Symptoms suggestive of vitamin D deficiency
- Increased risk of developing vitamin D deficiency in the future because of reduced exposure to sunlight, religious/cultural dress code, dark skin
- Raised PTH
- Medication with antiepileptic drugs or oral glucocorticoids
- Conditions associated with malabsorption.

Patients with a serum 25OHD above 50 nmol/L should be reassured and given advice on maintaining adequate vitamin D levels through safe sunlight exposure and diet.

Treatment of Vitamin D deficiency

The NOS guideline suggests that the key aims for treating vitamin D deficiency in patients with bone disease are to ensure correction of vitamin D deficiency and achieve a serum 25OHD >50 nmol/L, reverse the clinical consequences of vitamin D deficiency in a timely manner and to avoid toxicity. Vitamin D_3 (cholecalciferol) is the treatment of choice for most patients with vitamin D deficiency, as this is cleared less rapidly and is more bioavailable than vitamin D_2 (ergocalciferol) (6), but the latter my be preferred by vegetarians and patients who wish to avoid vitamin D of animal origin because of religious or cultural beliefs. Oral administration of vitamin D is recommended, because of unpredictable bioavailability and slower correction of vitamin D deficiency with

intramuscular preparations (7,8).

There are a number of different potential approaches to vitamin D treatment, ranging from daily supplementation to high dose annual dosing. Although the latter is convenient and maybe associated with good compliance with medication, a recent study suggests an increased risk of falls and fractures with single annual doses of 500,000 IU (12,500 μg) of vitamin D (9).

Where rapid correction of vitamin D deficiency is required, such as in patients with symptoms or those about to start treatment with a potent antiresorptive agent such as zoledronate or denosumab, the recommended treatment regimen is based on loading doses followed by regular maintenance therapy. Loading doses should provide a total of approximately 300,000 IU (7,500 μg) vitamin D, given either as weekly or daily doses. The exact treatment regimen will depend on the available vitamin D preparations but examples include:

- 50,000 IU (1,250 μg) given weekly for 6 weeks (total 300,000 IU; 7,500 μg)
- 40,000 IU (1,000 μg) given weekly for 7 weeks (total 280,000 IU; 7,000 μg)
- 4,000 IU (100 μg) given daily for 10 weeks (280,000 IU; 7,000 μg)

Maintenance treatment should be considered one month after loading, with doses equivalent to 800 to 2,000 IU (20 to 50 μg) vitamin D daily given either daily or intermittently at a higher equivalent dose. Where correction of vitamin D deficiency is less urgent and when co-prescribing vitamin D supplements with an oral antiresorptive agent, maintenance therapy may be started without the use of loading doses.

Monitoring of Vitamin D Treatment

As vitamin D treatment may occasionally unmask primary hyperparathyroidism, the NOS guideline recommends that protein adjusted serum calcium is checked one month after starting supplementation. Routing monitoring of serum 25OHD is not recommended but may be appropriate in patients with symptomatic vitamin D deficiency, or malabsorption and where poor compliance with medication is suspected.

Review of the NOS Guideline

Prior to the publication of the NOS guideline there was extensive stakeholder consultation with interested individuals and organisations. The guideline was endorsed by the Bone Research Society, British Dietetic Association, British Geriatrics Society, Royal College of Nursing, Paget's Association, International Osteoporosis Foundation, United Kingdom Clinical Pharmacy Association, Primary Care Rheumatology Society, Royal Pharmaceutical Society, British Orthopaedic Association, Society for Endocrinology, Arthritis Research UK and the Royal Society of Medicine. The guideline will be reviewed and updated if necessary in April 2016. A one page algorithm summarising the guideline is also available on the NOS website.
http://www.nos.org.uk/document.doc?id=1585

Contributor

All authors contributed equally to the guideline.

Competing Interests

The development of the guideline was funded by the NOS, but the authors received no fees for this work. Since the publication of the NOS guideline, RMF has served as an adviser to Internis, Consilient and ProStrakan. WDF has served as an advisor to Siemens, Becton Dickinson and Roche regarding 25OHD assay development. MKJ has been a speaker for Internis and served as an adviser to Consilient. HMM has served as an adviser to Internis and received vitamin D capsules from Pure Encapsulations for a research study of supplementation. PLS has served as an adviser to Internis.

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Provenance and peer review

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