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## Vitamin D levels in Hospice In-Patients: Clinical Audit

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## **Abstract**

**Objectives** Serum 25-hydroxyvitamin D will be obtained alongside routine blood tests in all suitable patients admitted to the St Cuthbert's Hospice Inpatient Unit for a period of 12 months. Supplementation will be offered to exclude vitamin D insufficiency or deficiency as a contributor to the complex pain and symptom profile of our patients.

**Methods** During admission, and alongside routine blood tests, a serum 25-hydroxyvitamin D test was requested for suitable patients. Supplementation was offered to patients with a serum 25-hydroxyvitamin D less than 50 nmol/L.

**Results** This audit identified that 79.73% of patients assessed had a 25-hydroxyvitamin D level less than 50 nmol/L and were therefore insufficient or deficient in vitamin D.

The results of the audit were discussed within the clinical team at the hospice and guidance changed to obtain serum 25-hydroxyvitamin D levels in all suitable patients. A re-audit highlighted that some patients were missed from testing and therefore reminders were sent to the clinical team.

**Conclusions** Most patients admitted to St Cuthbert's Hospice had either insufficient or deficient levels of vitamin D. It seems reasonable for all suitable palliative care patients to have their vitamin D level checked and to be started on a suitable dose of vitamin D replacement therapy.

## Key Messages

What was already known?

- Vitamin D has important roles beyond bone health.
- Supplementation has been linked to improved pain management and reduced infections in palliative care patients.

What are the new findings?

- Many palliative patients are insufficient or deficient in vitamin D and measurement of levels is often not routine practice.

What is their significance?

- Clinicians should consider measuring vitamin D alongside routine blood tests.

## Background

Vitamin D is a steroid prohormone obtained through sun exposure on the skin, food sources and supplementation. There are two major forms of vitamin D, commonly known as D2 and D3. Both vitamin D2 and D3 can be obtained from dietary sources, however vitamin D3 is synthesised in the skin from exposure to sunlight. Patients with insufficient exposure to sunlight are therefore at a higher risk of vitamin D deficiency.

It is well known that vitamin D regulates serum calcium and phosphate homeostasis. The Scientific Advisory Committee on Nutrition (SACN) have found evidence showing a positive benefit of vitamin D on musculoskeletal health including osteomalacia, falls, muscle strength and function.<sup>1</sup> Furthermore, vitamin D is involved in regulating gene expression, cell proliferation, differentiation and apoptosis.<sup>2</sup> It may also have an immunomodulatory effect through inhibition of TH1 cytokines and the generation of T regulatory lymphocytes and an antiproliferative effect.<sup>3</sup> The vitamin D activating enzyme CYP27B has been found in normal breast, colon, pancreas and prostate tissue as well as their tumours, supporting the potential link between increased cancer incidence and higher mortality levels in patients

with vitamin D deficiency.<sup>3-6</sup> Vitamin D supplementation has also been linked to improved pain management and reduced infections in palliative care patients.<sup>7</sup>

The vitamin D prohormone undergoes two enzymatic hydroxylation reactions before it becomes biologically active as calcitriol (1,25-dihydroxyvitamin D). The first step takes place in the liver, producing 25-hydroxyvitamin D and the second, converting to 1,25-dihydroxyvitamin D, in the kidney.<sup>8</sup> Measurement of serum 25-hydroxyvitamin D is used to assess vitamin D status, and the SACN has advised the risk of poor musculoskeletal health increases at levels below 25 nmol/L.<sup>1</sup> The National Osteoporosis Society (NOS)<sup>9</sup> and Institute of Medicine<sup>2</sup> guidelines highlights levels over 50 nmol/L as adequate, between 30 and 50 nmol/L as insufficient and less than 30 nmol/L deficient. Vitamin D3 has been found to be 87% more effective at increasing serum 25-hydroxyvitamin D than D2 and is commonly used for supplementation.<sup>10</sup>

## **Aims and objectives**

The aim of this audit was to measure serum 25-hydroxyvitamin D and exclude vitamin D insufficiency or deficiency as a contributor to the complex pain and symptom profile of patients admitted to St Cuthbert's Hospice Inpatient Unit, Durham, UK. Prior to March 2019, patients were not routinely assessed for serum 25-hydroxyvitamin D levels.

Serum 25-hydroxyvitamin D will be obtained alongside routine blood tests in all suitable patients admitted to the Inpatient Unit for a minimum of 12 months, beginning in March 2019. Supplementation will be initiated in patients with serum 25-hydroxyvitamin D levels below 50 nmol/L. A re-audit will then be conducted to determine testing rates following the initial audit.

## Standards

NICE CKS guidelines<sup>8</sup> state that patients should be tested if they are at higher risk of vitamin D deficiency, if they have chronic widespread pain, impaired physical function, have had a fall or if there is clinical reason to do so prior to specific treatment where correcting vitamin D deficiency is appropriate. The NOS<sup>9</sup> also states that it is important that people receiving potent anti-resorptive osteoporosis treatments (denosumab or zoledronate) are not vitamin D deficient before starting treatment, to reduce the risk of developing hypocalcaemia.

Palliative patients may receive these drugs prophylactically to reduce the incidence of bone metastases, to reduce bone pain and also to treat hypercalcaemia. Furthermore, there have been published benefits from vitamin D supplementation in cancer and palliative patients.<sup>5,6,11,12</sup>

This evidence was discussed by the clinical team at the hospice and it was deemed appropriate to therefore measure serum 25-hydroxyvitamin D levels in all suitable patients admitted to the inpatient unit. Patients who were considered to be too close to death to benefit from supplementation, or whose Australia-modified Karnofsky Performance Status (AKPS) was 20% or less were excluded from the audit.

NICE CKS guidelines<sup>8</sup> specify to treat for vitamin D deficiency if serum 25-hydroxyvitamin D levels are less than 25 nmol/L; however if the patient has a high fracture risk, is on a treatment linked to vitamin D deficiency or has a condition known to cause vitamin D deficiency then treatment should commence at levels below 50 nmol/L. Furthermore, the National Osteoporosis Society (NOS)<sup>9</sup> and Institute of Medicine<sup>2</sup> guidelines specify levels between 30 and 50 nmol/L as insufficient and less than 30 nmol/L deficient.

Given the often complex clinical background of many palliative care patients, this audit therefore identified patients with serum 25-hydroxyvitamin D levels less than 50 nmol/L. In these patients, where supplementation was clinically appropriate, it was initiated.

## **Methods**

The initial audit will run for a period of 12 months from March 2019 in order to obtain adequate and quality data to inform future policy at the hospice.

During admission, and alongside routine blood tests, a serum 25-hydroxyvitamin D test was requested for all suitable patients from the biochemistry laboratory at University Hospital North Durham.

All the patients who were deficient in vitamin D (serum 25-hydroxyvitamin D less than 30 nmol/L) were offered a loading dose of colecalciferol 40,000 IU a week for 7 weeks following NICE guidelines.<sup>5</sup> Those whose levels were in the insufficient range of between 30 and 50 nmol/L were offered a regular supplement of 800IU daily as per NICE guidelines. Advice was also given with respect to sun exposure during the summer months (April to September inclusive) and the importance of including vitamin D sources in the diet.

## **Results**

The audit ran for fourteen months between March 2019 and August 2020 and data was collected for 82 patients. There were two months where no data was collected, due to the disruption to practice caused by the COVID-19 pandemic. Eight of the tests sent were not analysed for various reasons including 'lab error', 'errors on the labelling of bottles' and 'COVID-19'. Out of the remaining 74 tests carried out, the results were as follows:

- 15 (20.27%) had a 25-hydroxyvitamin D level greater than 50 nmol/L, which is regarded as sufficient by the NOS.
- 12 (16.21%) had a 25-hydroxyvitamin D levels between 30 and 50 nmol/L which is regarded as insufficient by the NOS.
- 7 (9.46%) had a 25-hydroxyvitamin D level between 25 and 30 nmol/L which SACN regards as insufficient, and NOS regards as deficient.
- 40 (54.05%) had a 25-hydroxyvitamin D level less than 25 nmol/L which is regarded by both NOS and SACN as deficient.

This audit identified that 79.73% of patients had a 25-hydroxyvitamin D level less than 50 nmol/L and were therefore insufficient or deficient in vitamin D. These patients were prescribed appropriate supplementation as described above.

The results of the audit were discussed within the clinical team at St Cuthbert's Hospice and guidance changed to obtain serum 25-hydroxyvitamin D levels in all suitable patients. Supplementation will then be initiated as appropriate and in line with current guidelines.

In February 2021, the audit cycle was repeated over a period of four weeks. During this time 11 patients were admitted to the Inpatient Unit, of which 9 were deemed suitable to be included in the audit; seven of these were assessed for vitamin D levels and two were missed. Five of the seven patients who were assessed were insufficient or deficient and were started on treatment. Considering our aim is to test all suitable patients, reminders were sent to the clinical team in order to encourage increased testing rates.

## **Discussion**



NICE guidelines<sup>8</sup> suggest that everyone living in the UK should take a vitamin D supplement of 400IU daily to prevent deficiencies occurring. However, the experience at St Cuthbert's Hospice is that it is rare for the patients being admitted to the hospice to be taking a vitamin D supplement already. This may be due to lack of awareness of the necessity to do so, reluctance to increase tablet burden or symptoms preventing oral intake of anything but the absolutely necessary medication. Many of the patients being admitted have a complex array of symptoms which are often difficult to alleviate and this task may be made worse if the patient is deficient in vitamin D.

In addition to the benefits described earlier, Helde-Frankling M et al suggests that vitamin D can reduce pain through reducing pro-inflammatory PGE2 and Th1 and Th17.<sup>10</sup> Helde-Frankling also reports on a reduction in fentanyl use in a group of patients when they were given 4000IU/day of vitamin D where serum 25-hydroxyvitamin D levels were less than 75 nmol/L.<sup>7</sup> Moreover, B J Edwards et al<sup>12</sup> found that vitamin D levels correlated with overall survival in the elderly with solid tumours, with lower overall survival in those patients that were most deficient.

## **Conclusion**

The initial audit identified 79.73% of patients admitted to St Cuthbert's Hospice had either insufficient or deficient levels of vitamin D. It seems reasonable therefore for all suitable palliative care patients to have their vitamin D level checked and to be started on a suitable dose of vitamin D replacement therapy as per NICE guidelines and then continue on a maintenance dose thereafter.

More clinical studies in this field are needed before conclusions about the range of benefits of adequate vitamin D levels in palliative patients can be drawn.

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**Conflict of interest:** There are no conflict of interests to declare.

**Contributorship statement:** PL planned and designed the audit, including deciding upon inclusion criteria and appropriate 25-hydroxyvitamin D levels at which to initiate supplementation. PL conducted the audit and ensured all relevant patients were included. Both PL and KB were involved in a literature review and in analysing the results of the audit and its relevance to the literature and clinical practice within the hospice. KB wrote up the audit for dissemination and publication.

## References

1. Scientific Advisory Committee on Nutrition. SACN statement on nutrition and older adults living in the community 2021. Available at: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/953911/SACN Nutrition and older adults.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/953911/SACN_Nutrition_and_older_adults.pdf) Accessed on 04/03/21
2. Institute of Medicine Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Dietary Reference Intakes for Calcium and Vitamin D. Ross AC, Taylor CL, Yaktine AL, Del Valle HB, editors. Washington (DC): National Academies Press (US); 2011.
3. Adams JS, Hewison M. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. *Nat Clin Pract Endocrinol Metab.* 2008 Feb; 4(2):80-90. Doi: 10.1038/ncpendmet0716.
4. Townsend, K. Evans, K. Campbell, M. Colston, K. Adams, J and Hewison, M. Biological actions of extra-renal 25-hydroxyvitamin D-1 $\alpha$ -hydroxylase and implications for chemoprevention and treatment. *J Steroid Biochem Mol Bio.* 2005; 97:103-109. Doi:10.1016/j.jsbmb.2005.06.004.
5. Giovannucci, E. Liu, Y. Rimm, EB. Hollis, BW. Fuchs, CS. Stampfer, MJ. Willett, WC. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. *J Natl Cancer Inst.* 2006; 98(7):451-459
6. Zhou, Z. Ge, X. Fan, X. Wang, J. Miao, L. Hang, D. Associations of vitamin D status with colorectal cancer risk and survival. *Int J Cancer.* 2021; 10.1002/ijc.33580. doi:10.1002/ijc.33580
7. Helde-Frankling, M. Höijer, J. Bergqvist, J. Björkhem-Bergman, L. Vitamin D supplementation to palliative cancer patients shows positive effects on pain and infections - Results from a matched case-control study. *PLoS One.* 2017; 12(8):e0184208. Doi:10.1371/journal.pone.0184208

8. NICE Clinical Knowledge Summaries. Vitamin D deficiency in adults – treatment and prevention. December 2020. Available at: <https://cks.nice.org.uk/topics/vitamin-d-deficiency-in-adults-treatment-prevention/> Accessed on 11/03/21
9. National Osteoporosis Society. Quality Standards for Osteoporosis and Prevention of Fragility Fractures. November 2017. Available at: <https://theros.org.uk/media/0dillsrh/ros-op-standards-november-2017.pdf> Accessed on 11/03/21
10. Heaney, RP. Recker, RR. Grote, J. Horst, RL. AG Armas, L. Vitamin D<sub>3</sub> Is More Potent Than Vitamin D<sub>2</sub> in Humans, J Clin Endocrinol Metab. 2011; 96(3):E447–E452. Doi: <https://doi.org/10.1210/jc.2010-2230>
11. Helde-Frankling, M. Bjorkhem-Bergman, L. Vitamin D in Pain Management. Int J Mol Sci. 2017; 18(10):2170. Doi: [10.3390/ijms18102170](https://doi.org/10.3390/ijms18102170)
12. Edwards, BJ. Zhang, X. Sun, M. Song, J. Khalil, P. Sri Karuturi, M. et al. Overall survival in older patients with cancer. BMJ Support Palliat Care. 2020; 10:25-35. Doi: <http://dx.doi.org/10.1136/bmjspcare-2018-001516>