High Prevalence of Vitamin D Deficiency in Irish Patients with Hip Fracture

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Abstract

Background: Vitamin D is well recognized to be suboptimal in older patients and patients with fragility fractures are more likely to have lower serum vitamin D levels when compared to age-matched controls. Vitamin D deficiency is considered to be a serum level of 25-hydroxyvitamin D [25(OH)D] <50 nmol/L and a serum level >75 nmol/L is considered to be an optimal level. While international studies have demonstrated a high prevalence of vitamin D deficiency in patients who have sustained a hip fracture, there are no published studies on the prevalence of vitamin D deficiency in Irish patients who have fractured their hips.

Aim: To investigate the prevalence of vitamin D deficiency in consecutive patients admitted with hip fracture to a large Dublin Teaching Hospital. Methods: A prospective study over 12 months of all patients with a hip fracture admitted to a Dublin teaching hospital with measurements of serum bone biochemistry, 25-hydroxyvitamin D and parathyroid hormone levels.

Results: 156 patients admitted with an acute hip fracture were assessed over a 12 month period. 115 (67.3%) patients were vitamin D deficient (<50 nmol/L), with 14 (9%) patients having an optimal vitamin D level (>75 nmol/L). 27 (17.3%) patients were on vitamin D supplementation at the time of fracture with 10 (37%) still vitamin D deficient and only 8 (29.6%) of the supplemented patients having an optimal vitamin D level with no significant seasonal variation. Approximately one quarter of patients with vitamin D deficiency (<50 nmol/L) demonstrated secondary hyperparathyroidism.

Conclusions: This study confirms that there is a very high prevalence of vitamin D deficiency in Irish patients admitted to hospital with a hip fracture. Very few patients had optimal serum levels of vitamin D. Patients admitted on standard recommended vitamin D supplementation had higher mean serum vitamin D levels compared to non-supplemented patients but over a third were still vitamin D deficient and less than a third had an optimal level at the time of the fracture.

Keywords: Hip fracture; Vitamin D deficiency; Ireland

Introduction

Hip fractures are a major public health issue, which will become more common with the ageing of the population. Hip fractures are a cause of significant morbidity and mortality of older individuals. In most populations, hip fracture incidence increases exponentially with age [1,2] and is the most common clinical fracture for adults over the age of 75 years. At the end of the first year after a hip fracture, up to 50% of individuals have permanent functional disability, 15 to 25% require long-term nursing home care and up to 20% will have died [3-5]. In Ireland, it is estimated that 3500 to 4000 adults will sustain a hip fracture in a given year and this number is expected to increase in future years [6,7]. Identifying any potential treatable factor for a further hip fracture is of paramount importance and should be treated appropriately.

The importance of vitamin D status for optimal bone health has received increased recognition in recent years, with higher recommended vitamin D intake being proposed by some investigators [8,9]. Vitamin D deficiency is common among older adults and it is increasingly being recognised as a significant contributing risk factor for an osteoporotic fracture [10,11]. Vitamin D is required for the efficient absorption of calcium and for the normal mineralisation of bone. Serum 25-hydroxyvitamin D (25(OH)D) is the most common biomarker used to assess vitamin D status. Low serum 25(OH)D levels have been associated with an increased risk of falls and fractures in older adults [12]. This is thought to be mediated by its effects on bone metabolism and by contributing to an increased risk of falling. The risk of falling may be in part related to muscle weakness and to changes in balance [7,8]. There is a lack of consensus on the serum 25(OH)D concentration that reflects optimal vitamin D status, but a serum 25(OH)D concentration >75 nmol/L has been suggested as an optimal level for falls and fracture prevention [8].

Falls are a major component in fracture risk and fall prevention is a core part of the management of patients with fragile bones. The prevalence of falls increases with advancing age and is higher in females than in males [13-15]. Falls are a substantial factor in hip fractures. 95% of hip fractures are associated with a fall, with 10% of falls being associated with a fracture [16]. There have been several studies demonstrating the benefit of vitamin D in preventing falls [8,17]. This protective mechanism is thought to be related to improvements in muscle strength, as well as its effect on bone.

Ireland is at 53N latitude and its population risk vitamin D deficiency is high. The intake of vitamin D supplements has been associated with decreases in total mortality rates, and in line with international recommendations, the Irish public health authorities encourage the uptake by older people of regular vitamin D and calcium supplementation. Subgroups of the Irish population, including older adults and adolescent girls, have been shown to have a high prevalence
of vitamin D deficiency [18-20]. However, there is very little data on vitamin D status in patients with fractures in the Republic of Ireland. The aim of this study is to assess the prevalence of vitamin D deficiency in Irish adults who present with a hip fracture.

Materials and Methods

Subjects and setting

One hundred and fifty-eight subjects sustained a low trauma hip fracture between January 2008 and December 2008 inclusive. Two patients were excluded as they did not have a serum 25(OH)D level taken as both patients died in the pre-operative period. Of the 156 remaining patients assessed had serum taken for analysis (mean age 77.6, SD 10 years; 75.6% females). The mean age of female patients was 78.3 (SD 10) years and the mean age of males was 75.3 (SD 9.7) years.

A hip fracture was considered an osteoporotic fracture if it occurred due to low trauma. Low trauma fractures were either spontaneous or caused by minimal trauma (trauma equal to or less than a fall from a standing position). Informed consent was obtained from patients or their guardians. Patients with significant trauma or a history of metastatic carcinoma were excluded. Hip fractures were defined as any low trauma fracture of the femur between the articular joint of the hip and 5 cm below the distal point of the lesser trochanter. Admission records were reviewed on a daily basis with all patients being consented to physical examination and blood tests pre-operatively. The pathological hip fractures due to primary or metastatic bone cancer, multiple myeloma and Paget’s disease of bone were excluded. The study was approved by the local ethics committee. Written consent was obtained from all participants.

All patients who attended with hip fracture cases were identified using the in-hospital Electronic Patient Record System and theatre lists. Information on demographics, smoking, falls and medications (including vitamin D supplementation) was recorded. The history of previous fractures was ascertained by self-report, and no additional validation of this information was conducted.

All subjects were of ethnicity were White Irish, which makes the sample homogeneous for skin types. All subjects were ordinarily resident in Ireland. Travel histories (e.g. recent holidays at different latitudes) were not collected as part of the assessments. Sunlight exposure questionnaires were not used as there is evidence that they tend to provide imprecise estimates of vitamin D intakes [20,21].

25(OH)D and PTH measurements

All blood tests for serum 25(OH)D and PTH measurements were during acute care within 24 hours after the hip fracture event. Blood sampling was performed to analyse parathyroid hormone (PTH), 25-hydroxyvitamin D, serum creatinine, calcium, phosphate, albumin and alkaline phosphatase levels. Fasting early morning venous blood was collected from patients for the serum measurement. Samples were stored at -20°C. Serum samples were taken at the time of fracture with samples within 24 hours of the event and therefore it unlikely to be affected by the fracture, i.e. transient rises in serum calcium.

Serum 25(OH)D levels (in nmol/l) were analysed at St James’s Hospital Biochemistry Department using the DiaSorin Liaison 25-OH Vitamin D total (http://www.diasorin.com/en/productsandsystems/view/20), a chemiluminescence immunoassay. Inter- and intra-assay coefficients of variation were <12%. Internal quality control was deter- mined using kit controls of two different concentrations. The laboratory participates in the International Vitamin D External Quality Assessment Scheme (DEQAS, subgroup Liaison users) as a means of determining accuracy of results.

Vitamin D status was determined using kit controls of two different products and systems/view/20), a chemiluminescence immunoassay. LIAISON® 25-OH Vitamin D total (http://www.diasorin.com/en/James’s Hospital Biochemistry Department using the DiaSorin samples within 24 hours of the event and therefore it unlikely to be collected from patients for the serum measurement. Samples were fasting early morning venous blood sampling was performed to analyse parathyroid hormone (PTH), during acute care within 24 hours after the hip fracture event. Blood exposure questionnaires were not used as there is evidence that they aspire to provide imprecise estimates of vitamin D intakes [20,21]. Additionally, data on sunlight exposure was not collected as part of the assessments. Sunlight exposure questionnaires were not used as there is evidence that they tend to provide imprecise estimates of vitamin D intakes [20,21].

The mean serum 25(OH)D levels were 39.7 (± 25.5) nmol/L in the total group, 35.1 (± 22.1) nmol/L in the non-supplemented patients and 65.4 (± 28.2) nmol/L in the supplemented patients. Table 2 demonstrates 25(OH)D according to vitamin D supplementation group and pre-admission residence. Patients admitted from a nursing home had a lower serum vitamin D level compared to community dwellers (p=0.096). Non-supplemented patients admitted from a nursing home had significantly lower levels of serum 25(OH)D compared to non-supplemented community dwellers (p=0.005). 80% of nursing home residents had a serum 25(OH)D level less than 50 nmol/L.

Table 3 demonstrates the distribution of vitamin D levels within the study group. Severe vitamin D deficiency below 20 nmol/L was identified in 30.1% and below 50 nmol/L was identified in 67.3% of patients who are not supplemented with vitamin D and on vitamin D supplementation in the results.

Vitamin D supplementation

It was ascertained from the medication histories taken by the study physicians. Subjects were regarded as supplemented if they reported regular intake of prescription medicines and/or over-the-counter preparations (i.e. cod liver oil or multivitamin preparations) containing vitamin D.

Statistical analysis

We present unadjusted means for 25(OH)D levels by type of dwelling, season, and vitamin D supplementation group in Table 2. Continuous variables are expressed as mean ± standard deviation (SD) as well as median for parameter not normally distributed. A 0.05 level of significance was used throughout.

This was an observational, single centre study. It was conducted in accordance with the ethical principles of the Declaration of Helsinki, the Good Clinical Practice guidelines of the International Conference of Harmonization and local regulatory requirements and approved by the institutional ethics committee.

Results

Of the 156 participants that were assessed over the 12 months, 15 (9.6%) patients were admitted from a residential (nursing) home, with the remainder (141, 90.4%) being admitted from the community. Mean age of the participants was 77.6 (± 10) years, with the mean age of females being 78.3 (± 10) years and the mean age of males being 75.3 (± 9.7) years. 141 (90.4%) participants were admitted from home and 15 (9.6%) participants were admitted from nursing homes. 64 (41%) participants had a previous fracture at the time of the presentation with a hip fracture in this study. 27 (17.3%) participants were on vitamin D supplementation at the time of fracture, with 10.3% participants of vitamin D deficiency [18-20]. However, there is very little data on vitamin D status in patients with fractures in the Republic of Ireland. The aim of this study is to assess the prevalence of vitamin D deficiency in Irish adults who present with a hip fracture.
the overall group of patients. A greater percentage of male patients had serum vitamin D below 50 nmol/L compared to females (78.9% and 63.6%, respectively). 5% of non-supplemented patients achieved an optimum level of serum vitamin D (>75 nmol/L). 37% of supplemented patients had a vitamin D level below 50 nmol/L. Supplemented patients with a hip fracture had significantly higher serum 25(OH)D levels and had a higher prevalence of previous fracture. 73.6% of non-supplemented patients and 37% of supplemented patients had a serum 25(OH)D level <50 nmol/L.

The relationship between parathyroid hormone and 25(OH)D is demonstrated in Figure 1. Lower levels of serum 25(OH)D were associated with higher levels of parathyroid hormone with a significant correlation between the two variables, $r^2=0.0784$, $p<0.01$ (Figure 1). When comparing all individuals with a vitamin D level below 50 nmol/L, 23 of 105 (21.9%) had evidence secondary hyperparathyroidism (PTH >65 pg/mL, hospital standard range between 15-65 pg/mL). The remaining 82 patients with a 25(OH)D <50 nmol/L had a PTH level within the hospital standard reference range.

The seasonal variation in 25(OH)D levels was assessed in the group as demonstrated in Table 4. Serum 25(OH)D levels did significantly change in Summer and Autumn months compared to Winter months ($p<0.05$). Non-supplemented patients had low serum 25(OH)D levels throughout all seasons, indicating a high prevalence of vitamin D deficiency throughout the year. 86.8% of non-supplemented patients had serum 25(OH)D in Winter below 50 nmol/L. In Autumn months, 63.3% of non-supplemented patients had a serum 25(OH)D level <50 nmol/L.

### Discussion

In this sample of 156 consecutive Irish patients with hip fracture,
there was a high prevalence of vitamin D deficiency (25(OH)D <50 nmol/L) in Irish patients admitted with a hip fracture to a large Dublin hospital. 16.7% of patients were on any vitamin D supplementation at the time of fracture and 10.3% of patients were on the recommended on the 800IU per day according to guideline recommendations. Consequently, 25(OH)D serum concentrations were low in all subgroups with a high prevalence of severe vitamin D deficiency (<20 nmol/L) in 33% of individuals admitted from the community and 23% of individuals admitted from nursing home. The high prevalence of vitamin D deficiency is in general agreement with previous studies on the prevalence of vitamin D deficiency in fragility fracture populations [23-27]. The prevalence figures presented in this study, while reflecting a high prevalence of vitamin D deficiency, are similar to those from other studies in participants with fragility fractures in London [28], Belfast [29] and Glasgow [30] (mean serum 25(OH)D of 32.1, 36.1 and 35.2 nmol/L respectively). Romero-Ortuno et al. [22] has reported a high prevalence of vitamin D deficiency in Irish community-dwelling older people, with a mean 25(OH)D level of 40.3 nmol/L. A recent study of Indian patients with hip fractures and control patients demonstrated a high prevalence of vitamin D deficiency and secondary hyperparathyroidism with three fourths of the studied patients having vitamin D deficiency and a further having secondary hyperparathyroidism [23]. Our findings indicate that current guidelines on vitamin D supplementation for the prevention of falls and hip fractures in older adults are not sufficiently being practised.

Several studies have observed an increased serum PTH concentration in elderly people with or without hip fracture associated with vitamin D deficiency [31-33]. In our study, serum PTH correlated with levels of serum 25(OH)D, with higher levels of PTH being observed in those with lower vitamin D levels. Some studies have suggested that patients with the highest levels of PTH post hip fracture have poorer outcomes [34]. Patients with an elevated PTH compared to those with serum PTH in the normal range have a 15 times greater risk of fatal outcome and increased hospital stay [34]. Patients with hypovitaminosis D and secondary hyperparathyroidism compared to
those without elevated PTH levels have increased bone turnover [35-38], increased fracture risk [35] and a higher mortality rate, especially cardiovascular deaths [36,39]. Secondary hyperparathyroidism should be recognised as a significant risk factor for poor outcomes and should be treated.

A number of factors affect vitamin D levels including lifestyle, sunscreen usage, age and concomitant drug use. Endogenous production of vitamin D relies on 2 factors: solar UVB radiation penetrating the skin and the amount of 7-dehydrocholesterol in the skin. The amount of 7-dehydrocholesterol in skin is relatively constant until later in life, when it begins to decline [27]. Based on intervention studies, mean serum 25(OH)D levels in a vitamin D supplemented older population would be expected to be at least 50-60 nmol/L with a daily dose of 400 IU to 800 IU vitamin D3. The serum 25(OH)D levels in our study was consistent with published literature with mean serum 25(OH)D levels being 65.4 (+/-24.3) nmol/L in vitamin D supplemented patients as seen in Table 2.

In this study, there was no significant seasonal variation of serum 25(OH)D levels in non-supplemented patients, however, lowest levels serum 25(OH)D levels being observed in spring months and highest serum levels in autumn months. This seasonal variation has been observed in previous studies of healthy older adults [28,29] and hip fracture patients [30], although it has not been seen in all hip fracture patients [31]. This observation should be noted when prescribing vitamin D supplementation and is another area for further study in older patients. Seasonality and latitude are well documented causes of vitamin D deficiency and can influence levels [25,27]. However, in older adults the ability of the skin to produce vitamin D is reduced by several factors as previously mentioned. In countries above a latitude of 35°N, there is virtually no production of vitamin D from October to April, with populations being more reliant on oral supplementation for maintenance of adequate serum vitamin D levels [25]. In both the supplemented and non-supplemented groups, 25(OH)D seasonality was not detected, which may be accounted for by the small sample size.

Treatment of vitamin D deficiency not only preserves bone and muscle strength but also prevents falls and fractures [8,17]. Falls are a major component in non-vertebral fracture risk including hip fractures. Low levels of 25(OH)D have been linked to frailty and poor health status, which could contribute to an association with fractures [17]. Several studies have demonstrated the benefit of supplemental vitamin D3 in preventing hip fractures. Almost 20 years ago, Chapuy and Meunier [32] showed the benefit of 1200 mg calcium and 800 IU vitamin D3 in reducing the risk of hip fractures by 43% and the risk of non-vertebral fractures by 32% in institutionalised patients. The mechanism by which vitamin D reduces falls is thought to be through improvement of muscular strength and function. More recently in the NHANES III study, women >60 years of age with higher 25(OH)D levels were associated with improved lower extremity function (faster walking and sit-to-stand speeds) [33]. There have been several meta-analyses that have shown the value of vitamin D supplementation in preventing falls and fractures [34-36]. However, supplemental vitamin D in patients after a hip fracture remains controversial [37].

We noted that 1 in 6 (17.3%) of all patients were on vitamin D supplementation at the time of admission in the study group, with 10% of all the study group taking a recommended dose of 800 IU of cholecalciferol (Vitamin D3). A substantial portion of patients (41%) had a previous history of fracture at the time of admission. Previous fractures are a risk factor for having a hip fracture – this is particularly true for wrist and vertebral fractures [38]. This under-treatment of previous fractures is similar to a recent audit in the UK [39]. Better education of healthcare professionals, more consistent recording of fractures in primary care and the use of clearly defined care pathways that involve patients and their carers provide rational approaches to reducing this care gap.

There is much debate on the optimum level of serum vitamin D (25(OH)D). The International Osteoporosis Foundation (IOF) have published recommendations for the optimal serum 25(OH)D level to be above 75 nmol/L [9]. This serum 25(OH)D level is based on maximal PTH suppression, reduced rate of bone loss and falls to optimise overall bone health. The dose of vitamin D supplementation required by a patient would depend on several factors including the baseline level of serum 25(OH)D, body mass index, sun exposure and vitamin D metabolism. For individuals with effective sunlight exposure, a dose of 800 IU/day vitamin D3 may be sufficient. Patients with obesity, a history of falls, known osteoporosis and limited sun exposure may require higher doses of vitamin D3 up to 2000 IU/daily [9]. In our study, less than a third of the study patients achieved an optimal level of vitamin D on 800 IU vitamin D3/day which is the recommended daily intake of vitamin D. To achieve a higher serum vitamin D level, a higher vitamin D intake would be required. The rate of replacement, mode of administration and the total dose required for reaching optimal levels still remains to be fully established.

This is a cross-sectional study with consecutive patients from a Dublin teaching hospital being analysed. All patients were admitted from an urban setting and may therefore not be fully reflective of mixed rural and urban populations. This is a potential area for further research and it may be appropriate to repeat this study in several other centres to ascertain the national prevalence of vitamin D deficiency in Ireland in patients with hip fracture. A strength of the study is the assessment of seasonality, vitamin D supplementation and prior living residence as additional important determinants of 25(OH)D status in patients admitted with acute hip fractures.

In summary, our study shows a high prevalence of vitamin D deficiency in Irish patients presenting with an acute hip fractures and further efforts are needed to improve guideline practice for the prevention of hip fractures in Ireland. In addition, these patients also had a high prevalence of previous fragility fractures, with 41% reporting a previous clinical fracture. The results indicate that most community dwelling patients who have a hip fracture are vitamin D deficient at the time of the fracture. Identifying and treating patients who have vitamin D deficiency may reduce falls and fractures, and also reduce the incidence of secondary hyperparathyroidism with improvements in bone health. According to our analyses, desirable serum 25(OH)D concentrations of at least 75 nmol/l among older individuals at risk for hip fracture may only be achieved during the summer season with additional 800 IU vitamin D per day. In the winter season, 800 IU vitamin D may not be sufficient to raise serum 25(OH)D levels into the desirable range. There is a need for a heightened awareness of the high prevalence of vitamin D deficiency and the need to optimize vitamin D therapy amongst this older at risk group of patients.

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