Colecalciferol Initiation Post Minimal Trauma Fracture

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Abstract

Purpose: The purpose of this study was to determine the proportion of patients admitted to a major tertiary teaching hospital in Australia aged 50 years and older with a confirmed neck of femur or vertebral minimal trauma fracture, who are commenced on colecalciferol supplementation by discharge, and to describe the doses prescribed. **Methods:** A subanalysis of a retrospective audit of electronic medical files for patients admitted with a minimal trauma fracture of the hip or vertebra between January 1, 2016, and June 30, 2016, was conducted. **Results:** A total of 406 patients were screened and 64 patients were included in the audit. In this subanalysis of these 64 patients eligible for inclusion, 38 were not on any vitamin or mineral supplementation at admission. Of these, 26 patients (68.4%) had their serum colecalciferol levels measured, and 21 patients (55.2%) overall were initiated on colecalciferol. **Conclusion:** Over half of patients with a minimal trauma fracture were commenced on colecalciferol therapy, but a noteworthy proportion of patients remain untreated. Patients with colecalciferol levels are more likely to be initiated on therapy compared with those of whom levels were not taken during admission. This is a missed opportunity for intervention that may place patients at a higher risk of subsequent fracture; therefore, effective strategies should be implemented to address this treatment gap in the future.

Keywords

colecalciferol, cholecalciferol, vitamin D, osteoporosis, anti-osteoporosis therapy, osteoporosis treatment, minimal trauma, vertebral fracture, neck of femur fracture, femoral fracture

Introduction

Colecalciferol is important for bone health because it facilitates absorption of calcium, regulates calcium levels in the blood, and supports growth and maintenance of the skeleton.^{1–4} Falls and fractures have a large human and socioeconomic cost.² According to the World Health Organisation (WHO), the frequency of falls increases with age and frailty level.⁵ Older people who are living in nursing homes fall more often than those who live in the community.^{5,6} Approximately 30–50% of people living in long-term care institutions fall each year, and 40% of these patients experience recurrent falls.⁵ Watts et al, contends that the total direct and indirect costs of osteoporosis, osteopenia and associated fractures is predicted to be approximately A\$33.6 billion for Australians aged over 50 years over a projected 10 year period.⁷

Colecalciferol deficiency is common in Australia with over 30% of adults having a mild, moderate, or even severe deficiency.^{1,6} Low measurement of serum 25-hydroxyvitamin D (25(OH)D) levels can increase the risk of falls and bone fracture in older people.⁷ Thus, colecalciferol supplementation offers a strategy to reduce falls and fractures.

Studies have shown that supplementation can reduce the risk of falls and fractures by approximately 20%.^{7,8} A recent study determined that colecalciferol supplementation along with an annual medication review is a cost-effective intervention that reduces falls and provides health benefits in older adults living in assisted living facilities.⁹ Data of the effectiveness were derived from reviews of different trials. The interventions were defined as effective if they reduced the risk of injury after a fall or reduced the risk of falling.

The International Osteoporosis Foundation (IOF) recommends colecalciferol supplementation at 800 to 1000 IU/day for falls and fracture prevention in adults aged 60 years and older.^{8,10} Higher doses are recommended in those who are obese, malnourished, and have limited sun exposure or osteoporosis, and in high risk individuals, the IOF recommends measuring 25(OH)D and treating accordingly. Despite availability of evidence-based treatments, colecalciferol

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initiation rates of osteoporosis post minimal trauma fracture continue to be suboptimal.¹¹

This tertiary hospital audit site does not currently have a reliable process for the initiation of colecalciferol therapy post minimal trauma fracture, and anecdotal reports from clinical pharmacists suggest inconsistent practices for initiation between hospital units. Many patients are referred to their general practitioner for follow-up, and some patients receive no instructions. Therefore, the main purpose of this analysis was to establish the proportion of patients discharged from hospital with a minimal trauma fracture, who are commenced on, or have a plan to be commenced on colecalciferol supplementation.

Methods

Study Design

This study was a subanalysis of a retrospective inpatient file audit performed at 2 sites across a major tertiary teaching hospital in Victoria, Australia. All osteoporosis therapy data were collected by examining patients' electronic records. The inclusion criteria encompassed patients admitted for a vertebral or hip fracture with a discharge date during the specified 6-month period. Colecalciferol component of osteoporosis therapy is reported in this subanalysis.

Between January 1, 2016, and June 30, 2016, a list of potentially eligible patients was retrieved from a central database. These patients were screened and excluded if one or more of the following criteria applied: nonminimal trauma fracture; less than 50 years of age during admission; preadmission osteoporosis prevention therapy; palliative; died during admission.

Participants

The population chosen were those with femoral and vertebral fractures as these injuries tend to be associated with longer lengths of hospital stay, providing greater opportunity for prescribers to screen and initiate osteoporosis management. Traumatic fractures resulting from serious impact injuries, ie, motor vehicle accidents or violent assaults, are generally not associated with osteoporosis and were therefore excluded from this audit.⁴ Given that the objective of this project was to assess treatment initiation rates, those patients on colecalciferol prior to admission were excluded.

Outcome Measures

The primary outcome was to determine the proportion of patients commenced on colecalciferol therapy before or on discharge and to describe the specific doses of colecalciferol prescribed. The results are reported as a percentage of patients with colecalciferol levels taken during admission. Secondary outcomes attempted to compare colecalciferol

doses with the national recommendations and international guidelines, to analyze the potential relationship between serum 25(OH)D level and colecalciferol doses prescribed and to report whether there was a correlation between gender and colecalciferol initiation.

Data Collection

Data were obtained through the use of electronic systems, including scanned medical records using electronic content manager, pathology results system via clinical information systems, and the prescription dispensing system. Data were collected in 2 sections using a data collection tool: The first section investigated patients who did not meet exclusion criteria; the second section referred to patient parameters such as diagnosis and date of admission. A paper-based data abstraction instrument was utilized as the collection tool and subsequently entered into an electronic spreadsheet. This aided the standardization and reproducibility of this study and strengthens internal validity of the research. This was inexpensive and highly functional for this project as it involved multiple research sites.

Pharmacy students were recruited as auditors and allocated to work in pairs to ensure accurate data collection and minimize variability in data interpretation. The pairing of students also aided in reducing programmer input error in the setting of manual electronic data entry. The method for monitoring competence between these auditors included the supervision by a pharmacist for first 10 patients. Students successfully completed the audit collection tool for 10 patients to the standards of the supervising pharmacists before they worked unsupervised.

Data Analysis

Results from the data collection tool were analyzed manually using pivot tables in Microsoft Excel. The data were analyzed to obtain the number of patients commenced on colecalciferol therapy and the doses documented on discharge. Retrospective review of patients on colecalciferol prompted further investigation for colecalciferol levels during admission. All parameter analyses were expressed as percentages. All colecalciferol doses were expressed in international units (IU) and serum 25(OH)D levels reported as nmol/L.

Results

Patient Characteristics

Four hundred seven discharge episodes were recorded, with 1 patient readmitted; thus, a total of 406 patients were screened from hospital for a fracture of the hip or vertebrae between January 1, 2016, and June 30, 2016. Of the patients screened, 64 patients were eligible for inclusion (Figure 1). There was an approximately even division between recruitment of hip

Figure 1. Treatment initiation flowchart.

Table 1. Patient Characteristics (Number and Percentage Distribution of Study Population According to Age, Sex, Fracture Type, and Therapy Before Admission).

Patient characteristics (n = 64)	
Age	
Median	80 (53-94 years)
Sex	
Male	21 (33%) ^a
Female	43 (67%)
Fracture type	
Hip	37 (58%)
Vertebral	27 (42%)
Osteoporosis related therapy before admission	
Calcium	0 (0%)
Cholecalciferol	18 (28%)
Both	6 (9%)

^aPercentages rounded up to the nearest percentage value.

fracture patients to vertebral fracture patients with a median age of 80 years (Table 1). A further 26 patients were excluded due to colecalciferol treatment prior to admission. In 24 of these patients, colecalciferol was determined to be a preadmission medication, and 2 other patients did not have their preadmission medications adequately described.

Twenty-six of the remaining patients had a serum 25(OH) D level taken during their admission; of these patients, 5 were found to be replete, 18 patients were found to have a suboptimal level, and 3 patients were found to be deficient (Table 2). There were 12 patients who did not have their serum 25(OH)D levels taken during their admission; of these patients, 1 was prescribed colecalciferol on discharge and 11 did not receive colecalciferol on discharge.

Treatment Initiation

Overall, a total of 21 patients were prescribed colecalciferol on discharge, 20 of whom were prescribed therapy according to blood test results (Table 2). Replete serum 25(OH)D levels were found for 5 patients, with 2 of these patients receiving colecalciferol therapy despite this. There were 18 patients found to have suboptimal serum 25(OH)D levels, and 16 of these patients were newly initiated on colecalciferol by discharge. Finally, of the 3 patients found to be deficient based on their serum levels, 2 were initiated on colecalciferol. The remaining single patient did not commence treatment for an unspecified reason.

Doses of colecalciferol (Figure 2) varied with prescriptions ranging with daily doses of 1000 IU (9 patients), 2000 IU (2 patients), 3000 IU (4 patients), 5000 IU (3 patients); doses of 50 000 IU weekly (2 patients); and as part of a

Table 2. Colecalciferol Initiation in Males and Females.

	Male	Female	Total
Colecalciferol levels taken during admission	12	14	26
Replete (55-108 nmol/L) ^a	2	3	5
Prescribed	2	0	2
Not prescribed	0	3	3
Suboptimal (25-54 nmol/L)	8	10	18
Prescribed	7	9	16
Not prescribed	1	1	2
Deficient (<25 nmol/L)	2	1	3
Prescribed	1	1	2
Not prescribed	1	0	1
Colecalciferol levels not taken during admission	5	7	12
Prescribed	0	1	1
Not prescribed	5	6	11

^aParameters for colecalciferol reference ranges as defined by the clinical results viewer.

combination pack, which was equivalent to a 5600 IU weekly (1 patient). Although there are variations in consistency of prescribing practices with regard to colecalciferol based solely on serum concentrations, there is an overall trend of higher daily doses of colecalciferol prescribed to patients with lower serum levels in comparison with those who had higher serum levels (Figure 2). A marginally higher proportion of males were prescribed colecalciferol on discharge when compared with females (Figure 3) with 59% of males and 52% of females being prescribed colecalciferol.

Discussion

Colecalciferol supplementation following bone damage from minimal trauma fractures is an effective and simple method of sustaining bone health and preventing falls and future fractures, especially in the older population.¹ Fifty-five percent of patients who were discharged from the major Victorian tertiary teaching hospital aged 50 years and older with a confirmed fractured neck of femur or vertebral fracture were initiated on colecalciferol during their admission. The majority of these patients had their serum 25(OH)D levels taken during their admission with the exception of 1 patient who did not have a level-guided dose prescribed. While the fact that a majority of patients had serum levels guiding the initial dose of colecalciferol is encouraging, there is certainly room for growth and higher rates of compliance. Ideally, all patients in this particular population should have levels available to aid in clinician decision making.

The recommended guidelines (Table 3) vary depending on patient-specific characteristics (ie, age, dark skin, projected day-to-day sun exposure, etc); in the older population, a dose of at least 1000 IU per day is recommended to reduce

fracture risk.⁸ Recommendations for treatment of colecalciferol deficiency vary from 3000 to 5000 IU per day for at least 6 to 12 weeks, to 50 000 IU per month for 3 to 6 months with intent to decrease to an ongoing maintenance dose of 1000 IU per day after the period of loading with colecalciferol.¹²

In addition, colecalciferol replete individuals are unlikely to benefit from continued high colecalciferol doses. Excessive doses of colecalciferol supplements (not from direct sunlight) in these individuals may lead to toxicity.^{12,13} Despite this, relatively high doses have been proven to be safe and are even recommended in some patient populations.¹²⁻¹⁴ Colecalciferol has been reported to have increased risk of toxicity in doses greater than 10 000 IU per day.¹⁵

There were 2 patients who had been prescribed the equivalent of 7000 IU per day (50 000 IU weekly), 1 of whom had a documented loading plan and intention to decrease regimen to a maintenance dosage. It is improbable that such a high prescription would be intended to continue for longer than a few weeks; however, there was no plan documented for the second patient.

Higher serum 25(OH)D levels predictably correlates to a lower daily dose of colecalciferol (Figure 2). The majority of patients included in this study were discharged on 1000 IU of colecalciferol per day, and all patients who were prescribed higher doses per day of colecalciferol were those found to have serum levels of less than 50 nmol/L. This indicates a general trend of appropriate colecalciferol prescription where levels are available via the pathology viewer.

It would be expected that 25(OH)D levels would be one of the more highly requested results from the pathology services in this patient population. Based on the parameters of our study, 68% of patients admitted had their serum 25(OH)D results available during admission; while this is a promising outcome, there appears to still be room for improvement. However, this audit does not account for levels being available to the treating clinician via other means. These may include, but are not limited to, inclusion with referral paperwork from the general practitioner or other transferring hospital; or pathology tests performed recently in the community and obtained by the clinical team by request. Our expectations would be that all new prescriptions of colecalciferol would be guided by levels. Based on our results, only 1 patient who did not have their 25(OH)D levels taken was initiated on colecalciferol. Although this result does not account for the fact that the patient may have had their serum 25(OH)D levels taken elsewhere, these results support the practice that the majority of colecalciferol prescribing at this hospital is guided by levels.

Conversely, 29% of patients did not have serum 25(OH)D levels taken and was discharged without a prescription of colecalciferol by discharge. This proportion may be an overestimate as a number of contributing factors could have precluded any single patient from taking colecalciferol. Our audit did not concentrate on specific patient factors such as patients personal preference to refuse therapy,

Figure 2. Effect of serum 25-hydroxyvitamin D levels on prescription of colecalciferol dose with trend line.
Note. Various dosing regimens for colecalciferol were prescribed. Doses prescribed weekly or monthly were converted to an equivalent daily dose to allow for comparison. All doses were rounded to the nearest thousand. IU = international units.

Figure 3. Proportion of colecalciferol initiation in the (A) female and (B) male study population.

Table 3. International Osteoporosis Foundation's Recommendations for Colecalciferol Therapy.

People obtaining some sun exposure but not at recommended level	Under 70 years at least 600 IU per day
Sun avoiders or people at risk of colecalciferol deficiency	Over 70 years at least 800 IU per day
Moderate to severe colecalciferol deficiency	Higher doses may be required
	1000-2000 IU per day
	3000-5000 IU per day for 6-12 weeks to raise the level of colecalciferol quickly, followed by a maintenance dose of 1000-2000 IU per day as advised by a doctor

Note. IU = international units.

the presence of administration complications, previously failure therapy attempts (in that event, if other options of colecalciferol therapy were trialed i.e. liquid formulations, etc.).

Serum levels allow clinicians to have objective ranges to aim for. Despite this, there is an aspect of subjective and

clinical judgment involved in prescribing. Levels may only act as a guide to colecalciferol initiation. For the most part, the prescription of colecalciferol was in accordance with levels; there were only 3 instances in which colecalciferol was warranted based on serum levels (ie, serum levels were deficient or suboptimal) but was not prescribed.

The first 2 instances were in patients who would have ideally benefitted from initiation of therapy (25(OH)D level of 24 nmol/L and 36 nmol/L, respectively), the reason behind colecalciferol nonprescription was not documented. The third instance was in a patient who had a serum 25(OH)D level of 53 nmol/L, which, by the reference ranges specified in the pathology system, was suboptimal but on the cusp of being classified as replete (Table 2). It can be inferred that this instance was an example of where clinical judgment was used. There is conflicting evidence as to the optimal level of serum 25(OH)D and recommendations may vary from as low as 50 nmol/L up to 75 nmol/L.^{13,15} Therefore, depending on the training of the clinician and the reference used, a serum 25(OH)D level of 53 nmol/L can be interpreted as an adequate level and colecalciferol supplementation was not required.

Results (Figure 3) conclude that males were more often prescribed colecalciferol therapy when compared with females. Hormonal changes can exaggerate colecalciferol deficiency,¹³ as such, females in particular are at a higher risk of developing osteoporosis given the drastic hormonal shift that occurs with menopause,^{16,17} and it is of particular importance to initiate treatment in this population because of this risk. Due to the risk in this population, initiation rates in females would preferably be significantly higher than that of males and given these moderate results, this is an aspect that requires some improvement and represents a gap in existing therapy.

Limitations

There were several limitations identified. First, only a small sample size was eligible for inclusion. The majority of the patients excluded from the study were admitted to this hospital for a high-impact vertebral fracture, often as a result of a motor vehicle accident. Therefore, collecting data retrospectively from patients who were admitted for a hip fracture over a longer period of time would provide a larger sample size and more significant results. With this in mind, the inclusion of vertebral fracture patients has added value to the results. If vertebral fracture patients were initially filtered to exclude those admitted for a moderate or high-impact trauma fracture, more time would have been available to audit an extended retrospective period. This may have resulted in a greater proportion of fracture patients who were ultimately included in the study.

Second, fractures of the wrist due to minimal trauma are the most common symptomatic fracture related to osteoporosis.¹⁸ Patients admitted to the hospital for a wrist fracture were not included due to time limitations available for auditing. In addition, these patients are often assessed by the hospital's emergency department and not admitted as inpatients. Therefore, the short length of stay for these patients resulted in an inability to capture sufficient data for the purposes of the study.

Third, each patient included in the study had a single initial reading of serum 25(OH)D level recorded and subsequent

levels (if any) were not recorded for the purposes of the study. Moreover, the length of stay for each patient was not a point of comparison; as such, colecalciferol doses on discharge were compared regardless of duration of hospital stay. Patients who had an initial reading of "deficient" or "sub-optimal" may have appropriately commenced on a higher dosing regimen but subsequently had an extended admission that surpassed the loading period and were discharged on the maintenance dose, or had therapy discontinued. In these instances, it may have resulted in underrepresentation of correct and appropriate prescribing practices at this hospital.

Furthermore, the study design is retrospective and therefore some assumptions were made, particularly regarding the inpatient information provided. The scanned medical record was a recent implementation at this particular hospital and, as a result, some patient records were incomplete. In addition, when a medication management plan was not uploaded to a patient's file, the medication list and medical history on the discharge summary was used as an alternative source to obtain information regarding patients' medical history prior to their admission. This resulted in some inconsistencies in the sources used to obtain information between patients. The discharge summary information provided to the patient's general practitioner for review upon discharge was assumed to be accurate.

Finally, the interpretation of whether the patient's fracture was due to a minimal trauma was assessed on an individual basis through the information available in the medical admission notes. At times, the extent of the impact of trauma was unclear, and this resulted in difficulties determining whether or not the fracture met the predetermined definition of a minimal trauma fracture. To reduce bias during this process, all data were analyzed jointly by 2 auditors and validated by a third person independently.

Conclusion

While over half of patients presenting to this major Victorian tertiary teaching hospital with a minimal trauma fracture were commenced on colecalciferol therapy, there still remains a proportion of patients who did not have levels taken nor receive colecalciferol therapy. This represents a missed opportunity for intervention that may place patients at a higher risk of subsequent fracture; therefore, effective strategies should be implemented to address this treatment gap in the future.

Serum 25(OH)D levels guided dosing where these results were available. Patients who had a level taken through the pathology services at the hospital correlated to a greater likelihood of colecalciferol initiation. A higher level appropriately corresponded to a lower colecalciferol dose or no colecalciferol being prescribed. Most prescriptions were consistent with national recommendations and international guidelines. Interestingly, gender seemed to have little to no influence on the probability of colecalciferol prescription.

Clinicians are demonstrably recognizing that colecalciferol is of importance, with the majority of patients who had serum 25(OH)D levels taken at the hospital also initiated on therapy by the time of discharge. However, there remains a significant need for intervention with colecalciferol supplementation in the minimal trauma fracture patient population and as such all patients should have serum 25(OH)D levels requested.

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