

Prevention of glucocorticoid-induced osteoporosis: a re-audit of dual-energy x-ray absorptiometry scan access and management guideline compliance

Aim: To evaluate the current use of bone densitometry and agents to prevent glucocorticoid-induced osteoporosis. In 2004 we undertook a similar audit which showed poor adherence, and problems highlighted during that audit were lack of awareness and no access to public dual-energy x-ray absorptiometry (DEXA) facilities. Staff awareness was increased by local presentations and arrangements were made to have access to DEXA scans. This 2009 re-audit was carried out in order to establish what improvements in care had occurred in the intervening 4 years. **Methods:** A chart review was conducted for all patients seen in rheumatology outpatient departments, for a period of 8 weeks. Patients, prescribed any individual dose of glucocorticoids for more than 3 months, were identified and their medical records were audited. **Results:** Only 3.58% of patients were identified taking glucocorticoids for more than 3 months, versus 6% in 2004. In the over 65 years age group, none had a DEXA scan and 95% were on appropriate prophylaxis, versus 67% in 2004. In the under 65 years group, none had a pathological fracture history; only 38% of patients had a DEXA scan and were on appropriate treatment, versus none in 2004. Only 29.4% of patients were prescribed steroids for inflammatory joint disease, versus 61.7% in 2004. Overall, 74% of patients were appropriately managed as per recommended guidelines versus only 26% in 2004. **Conclusion:** A major improvement was noted in the management of glucocorticoid-induced osteoporosis; however, service deficiencies tend to persist.

KEYWORDS: DEXA scan ■ glucocorticoids ■ guidelines ■ osteoporosis

Since inflammation plays a key role across the spectrum of rheumatologic diseases, glucocorticoids are commonly used in patients with rheumatic symptoms. Approximately 75 million people in Europe, the USA and Japan suffer from osteoporosis [1], and glucocorticoid treatment accounted for more than half of the cases of osteoporosis identified in young people in one study [2]. The prevalence of the use of glucocorticoids in a community-based population was noted to be approximately 0.5–0.9% [3,4]. To reduce this risk of iatrogenic osteoporosis, guidelines were developed jointly by the Royal College of Physicians of London, the Bone and Tooth Society and the National Osteoporosis Society and were published in December 2002 [5]. As per these guidelines, osteoprotection should be offered to those who are above the age of 65 years or have previous fragility fractures (without the requirement for BMD measurement). For the under 65s, management is based on dual-energy x-ray absorptiometry (DEXA) scan measurements; treatment should be offered if BMD T-score is less than or equal to -1.5, and a repeat BMD measurement is suggested for those with a BMD T-score of more than -1.5. Many studies show that the majority of patients treated with steroids do not receive appropriate treatment to prevent bone loss [3,6].

We sought to investigate the compliance to international guidelines for management of glucocorticoid-induced osteoporosis (GIO) and to improve our clinical practice by raising the awareness of osteoporosis prophylaxis by conducting an audit in corticosteroid-treated patients in our regional rheumatology center. We also tried to elucidate whether limited access to DEXA scanning makes any difference in the management of patients taking chronic corticosteroids, as availability of DEXA scanning is very limited to public patients in the Waterford Regional Hospital catchment area. In 2004, we undertook an audit with the aforementioned objectives. This revealed poor adherence to the guidelines and problems highlighted were lack of awareness and no access to DEXA scanning. Staff awareness was increased by local presentations and arrangements were made to have, at least, limited access to DEXA. In 2009, we undertook a similar audit in order to establish what improvements in care had occurred in the intervening 4 years.

Methods

We conducted an 8-week prospective survey of all clinical notes of patients attending our regional rheumatology outpatient clinics.

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Patients on any strength of glucocorticoids for 3 months or less were identified, and their medical records were audited for demographic data, dose and duration of steroid usage, diagnosis, any fragility fractures, any DEXA scan organized and whether any prophylaxis against GIO was prescribed. The information regarding the prevalence of pathological fractures was based on the review of medical records and patient's self-report. Serum 25(OH)-vitamin D levels were not measured as a part of this audit. All such patients were regularly advised to take adequate amounts of calcium (at least 1200 mg per day) and vitamin D (800–1000 IU per day), and this supplementation was not based on vitamin D biochemical assay. Patients receiving short courses (<3 months duration) of glucocorticoids were not included in this study. This audit was carried out on consecutive patients who attended our regional general rheumatology clinics over 2 months, from May to the end of June 2009. Study patients ranged in age from 20 to 79 years with a mean of 62 years (± 11.5); 64% of the cohort was female. The study was conducted in adherence with the Declaration of Helsinki and International Committee on Harmonization good clinical practices. Findings were compared with the results of the previous audit. The audit was not designed to assess the quality of guidelines but the performance of our rheumatology unit according to these guidelines.

Results

A significant change was noted in the pattern of bone mass measurement and use of bone-protective medications between 2004 and 2009 among rheumatology patients receiving continuous glucocorticoid therapy for more than 90 days. Overall, 949 patients were reviewed during the audit period (2009); only 3.58% ($n = 34$) were identified taking glucocorticoids for more than 3 months, versus 6% in 2004. A total of 62% ($n = 21$) were 65 years of age or older. The guidelines recommend that these patients should be prescribed osteoprotection and BMD measurement is not required for this particular group of patients. None of the patients in our cohort (≥ 65 years of age) had a DEXA scan and 95% were on appropriate prophylaxis (calcium [at least 1200 mg per day], vitamin D [at least 800 IU per day] and bisphosphonates), versus 67% in 2004.

A total of 38% of the whole cohort ($n = 13$) were under the age of 65 years and the guidelines suggest treating such patients depending on their BMD measurements. None of these patients

had any known pathological fractures; however, only 38% (five out of 13) of such patients had a DEXA scan and were on appropriate treatment, versus none in 2004. Out of those 62% (eight out of 13) of patients who had no BMD measurement, 75% ($n = 6$) were on pharmacological prophylaxis against GIO (calcium, vitamin D and bisphosphonates) and the rest were not prescribed any prophylaxis. None of the young patients were assessed for gonadal dysfunction. Overall, 74% (25 out of 34; 20 patients in the >65 years age group and five in the <65 years of age group) of patients were properly managed as per recommended guidelines versus only 26% (12 out of 47; all were aged ≥ 65 years) in 2004. TABLE 1 summarizes these results. There was no documentation in medical records of any contraindication to bisphosphonates among those patients who were not prescribed medications to prevent bone loss. TABLE 2 shows the underlying diseases for which glucocorticoids were prescribed. An interesting observation was made that, overall, only 29.4% of the patients were prescribed steroids for inflammatory joint disease, versus 61.7% in 2004 ($p = 0.005$), revealing a significant drop in the trend to prescribe long-term glucocorticoids for inflammatory joint diseases.

Discussion

Since their discovery in 1949, the glucocorticoids are among the most widely prescribed drugs for the management of several inflammatory conditions. It is well documented that glucocorticoids have potent anti-inflammatory and immunomodulatory properties. There is a major concern that beneficial effects of glucocorticoids are overshadowed by the several predictable and serious complications. The most important of all these is GIO, due to its association with significant morbidity, mortality and socioeconomic impact. Glucocorticoids are used in approximately 0.5–0.9% of the population at any given time and fractures may occur in 30–50% of the patients on chronic glucocorticoid treatment [7]. A recent meta-analysis of prior corticosteroid use and fracture risk indicated that the risk of all fractures is substantially greater in GIO than in postmenopausal osteoporosis [8]. An extensive survey of general practice in the UK revealed that only 14% of patients taking oral steroids had received any treatment to prevent or treat osteoporosis [3]. Owing to concerns over the risks associated with long-term glucocorticoid use, its use is generally advisable as a short-term rescue therapy, or as a bridging therapy for different DMARDs. Glucocorticoids have a biphasic effect on bone,

Table 1. Changing patterns in prescribing glucocorticoids in two age groups, from 2004 to 2009.

	2004 (% of total patients)	2009 (% of total patients)	p-value
Total number of patients on chronic glucocorticoids	6 (n = 47)	3.58 (n = 34)	
Patients aged ≥65 years	38 (n = 18)	62 (n = 21)	
≥65 years of age, on appropriate treatment	67 (n = 12)	95 (n = 20)	0.018
≥65 years of age, had DEXA scan	None	None	
Patients aged <65 years	62 (n = 29)	38 (n = 13)	
<65 years of age, had DEXA scan	None	38 (n = 5)	
<65 years of age, had no DEXA scan, even though on osteoprotection	41 (n = 12)	46 (n = 6)	0.773
<65 years of age, having any low fragility fractures	None	None	
Overall, on appropriate management as per guidelines	26 (n = 12)	74 (n = 25)	<0.000

DEXA: Dual-energy x-ray absorptiometry.

initially stimulating bone resorption, leading to a large decrease in BMD; and then, after long-term continued use, suppressing the bone formation, leading to a smaller decrease in BMD [9]. Hence, the most rapid bone loss occurs in the first 6–12 months of systemic glucocorticoid therapy, but bone loss continues at a slower pace with more prolonged therapy.

Densitometric measurement of bone mass remains central not only in diagnosing osteoporosis, but also in determining a fracture risk. Low BMD is associated with all types of fractures. DEXA is the common and most readily available method to measure bone density and is considered as the gold standard for diagnosing osteoporosis. Other techniques include quantitative computed tomography and ultrasonography. Recently the National Osteoporosis Foundation [101] released its updated guidelines on therapy for osteopenia and osteoporosis, and this information is based on the long-awaited WHO algorithm Fracture Risk Assessment Tool (FRAX®) [102]. This algorithm estimates the likelihood for a person to have a major fracture over a period of 10 years. This will considerably change the way we evaluate and treat patients, both men and women, who may be at risk for fractures from osteopenia or osteoporosis. This tool takes into account more than just the BMD; it looks at current age, gender, ethnicity, family history and personal history of fracture,

femoral neck bone density, BMI, long-term use of glucocorticoids, intake of more than 3 units of alcohol a day, current smoking, disorders associated with secondary osteoporosis and rheumatoid arthritis. The FRAX will not replace the traditional bone density scan; rather, it integrates the weight of clinical risk factors for fracture with or without information on BMD. Hence, when used in conjunction with BMD measurements, it could change the recommendations the physician makes about whether a patient should require therapy for osteopenia or osteoporosis. Adding this risk assessment tool into the DEXA software will greatly increase the likelihood that need for therapy is properly evaluated.

It is important to highlight that vertebral fractures are the most common of all osteoporotic fractures [10], and studies have shown that asymptomatic vertebral fractures are common in patients receiving long-term glucocorticoids [11]. In the context of prophylaxis against GIO, their detection significantly changes the threshold of pharmacological intervention in such patients. Anteroposterior and lateral views of the thoracic and lumbar spine are the most important views for the assessment of osteoporotic deformity. Moreover, new techniques have been developed to assess vertebral fractures on DEXA images, which are known as ‘instant vertebral assessment’ (IVA) or ‘vertebral fracture assessment’

Table 2. Medical conditions for which glucocorticoids were prescribed.

Disorder	2004 (% of total patients)	2009 (% of total patients)
Rheumatoid arthritis/seronegative arthritis	62 (n = 29)	29 (n = 10)
Polymyalgia rheumatica/giant cell arteritis	32 (n = 15)	50 (n = 17)
Myositis	2 (n = 1)	6 (n = 2)
Systemic lupus erythematosus	4 (n = 2)	12 (n = 4)
Adult still disease	0	3 (n = 1)

(VFA). For the identification of patients with fracture, visual assessment of such DEXA scan images had 100% sensitivity and specificity [12]. Hence, with their low radiation and good precision, IVA/VFA could be utilized as a prescreening tool during the DEXA assessment, and if positive, these fractures should be confirmed by x-rays of the thoracic and lumbar spine.

We present an audit on osteoporosis prophylaxis in a typical population of rheumatology patients. This audit originally (in 2004) highlighted a variety of potential problems, including awareness issues and service deficiencies as there was no access to DEXA scan. A variety of measures were discussed to raise the awareness of this potentially treatable complication. Local medical and nursing staff were informed of the results, and the results were also presented at the annual meeting of the Irish Society of Rheumatology in 2004. By re-auditing in 2009, we have found that there has been a major improvement regarding the awareness of guidelines especially for patients over 65 years of age. The Royal College of Physicians guidelines also suggest that all patients at risk of osteoporosis who are under the age of 65 years should have a DEXA scan. In 2004, there was no public access to DEXA scan facilities and, not surprisingly, none of the patients under the age of 65 years were appropriately treated according to the guidelines. This led to new arrangements to provide access to DEXA facilities, but unfortunately this remained limited. In 2009, our re-audit reveals that we are still quite far from achieving the standard, and a major hindrance remains the lack of open access to DEXA scan. It has already been shown that access to bone densitometry does affect the medical practitioner's decision to prescribe osteoporosis treatment in high-risk steroid users [13]. Continuing deficiencies in the resources available pose a significant risk towards effective care for patients on long-term glucocorticoids.

In our audit, we noted a significant drop in the intervening 4 years of prescribing maintenance steroids for inflammatory joint diseases. A plausible explanation could be the availability of next-generation DMARDs – biologic agents, such as TNF inhibitors, costimulatory modulators, B-cell depletion therapies and anti-IL-6 therapy. In contrast to previous studies, it was reassuring that in our cohort there was quite a low percentage of patients on oral corticosteroids, even though we included all patients who were on oral corticosteroids regardless of

the strength. A 2002 regional audit in the UK showed that 13.3% of their patients were taking oral corticosteroids, when patients using over 7.5 mg of corticosteroids were recorded [14]. In Ireland, a recent audit in 2007 showed that 7% of patients were using chronic glucocorticoids, when patients taking at least 5 mg of glucocorticoids were audited [15]. There are limitations to this study. For example, the audit was carried out over a short period of time, involving only a few patients taking corticosteroids. Moreover, full data collection detailing additional risk factors (besides being on corticosteroids) for osteoporosis was not performed. However, these notable limitations were never meant to be the focus of this audit. Rather, we wanted to gain a snapshot of the compliance to international guidelines for the management of corticosteroid-induced osteoporosis, and also by closing the audit loop, we attempted to establish what improvements in care had occurred in the intervening years. In an attempt to minimize the selection bias, we recruited all consecutive patients reviewed during the audit period.

Conclusion

The results of this re-audit reveal that in the intervening 4 years there has been a major improvement regarding the awareness of guidelines, especially for the over 65 years of age group. For patients under the age of 65 years, the guidelines recommend BMD measurement and then treating or rescanning accordingly. As DEXA scan availability is limited in our regional center, we are uncertain whether we are overtreating those patients who are on osteoprotection or undertreating those who are not prescribed with osteoporosis prophylaxis. Therefore, we conclude that in our regional center, limited access to DEXA facilities continues to hamper effective management of GIO. To follow these guidelines, rheumatologists and other specialists prescribing glucocorticoids should have better access to DEXA facilities.

Future perspective

Appropriate management of GIO requires either revision of existing guidelines to abolish the need for DEXA or better access to DEXA facilities. Testosterone replacement therapy has been shown in small studies to improve spinal BMD in patients on chronic corticosteroids; however, further evidence is required. It is hoped that newly approved and investigational agents, such as once-yearly zoledronic acid (a bisphosphonate), teriparatide injections (a parathyroid

hormone drug) and 6-monthly denosumab (a fully human monoclonal antibody to the RANK ligand) would help clinicians in the management of patients with GIO, which remains vital given the commonness of glucocorticoid use and its associated morbidity and mortality. Patient and primary care physician education is imperative to achieve the uphill task of implementing and adhering to evidence-based guidelines.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter

or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Executive summary

- Glucocorticoids are the most common cause of secondary osteoporosis and different guidelines are available for its prevention.
- We investigated the appropriate management of glucocorticoid-induced osteoporosis against international recommendations (by the Royal College of Physicians of London).
- We closed the audit loop by re-auditing patients on chronic glucocorticoids.
- Overall, 74% of patients had appropriate management as per guidelines versus 26% in 2004 ($p < 0.0001$).
- Service deficiencies persist, and despite the availability of international recommendations, adherence to guidelines for managing glucocorticoid-induced osteoporosis remains suboptimal.

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■ Websites

- 101 National Osteoporosis Foundation www.nof.org/professionals/pdfs/NOF_ClinicianGuide2009_v7.pdf
- 102 WHO Fracture Risk Assessment Tool www.shef.ac.uk/FRAX/