The prevention and treatment of glucocorticoid-induced osteoporosis in clinical practice

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ABSTRACT – Glucocorticoids are associated with increased risk of bone loss and fracture. This study compared the prescribing of bone protective agents by rheumatologists in clinical practice with the standards recommended in the 1998 UK Consensus guidelines. All glucocorticoid users who attended rheumatology outpatients during a four-week period were eligible. Notes were audited according to a predefined proforma. Among the 1,290 rheumatology outpatients seen in the study period, 189 (15%) were taking glucocorticoids. 63% of glucocorticoid patients were taking calcium and 46% vitamin D. In total, 124 (71%) of the 175 patients available for review were at high risk of osteoporotic fracture, of whom 76 (61%) were taking appropriate prophylaxis. In 26 (15%) patients, insufficient information was available to be able to quantify the risk of fracture. The study showed that the audit standard was not met in 39% of cases. A better strategy for the monitoring of clinical risk factors is therefore required.

KEY WORDS: glucocorticoid-induced osteoporosis, guidelines, prophylaxis

Introduction

Prolonged oral glucocorticoid therapy is associated with accelerated bone loss[1] and an increased propensity to fracture.[2–5] The bone loss is dependent on both the daily dose and duration of treatment[6] and even relatively low doses (for example, 2.5 mg prednisolone daily or equivalent) result in increased skeletal loss and elevated fracture risk.[5,7]

Glucocorticoids are used to treat a wide variety of chronic inflammatory rheumatic conditions, including rheumatoid arthritis and connective tissue disease. Thus, glucocorticoid-induced osteoporosis has become increasingly important to rheumatologists and their patients. Previous studies have shown that the vast majority of glucocorticoid-treated patients have not been evaluated for osteoporosis risk or commenced on treatment to prevent accelerated bone loss and future fracture.[8–15] Rheumatologists are among those with the greatest experience of glucocorticoid therapy, and are also most likely to report that they would prescribe preventive therapy.[16] A survey of medical inpatients in Australia suggested that rheumatological patients taking glucocorticoids were more likely to have been offered bone density screening and/or prophylactic treatment than were similar patients with respiratory disease.[17] However, surveys of practice among rheumatologists in Canada,[18] the USA[19] and the UK[20] revealed considerable variability.

During the past decade, increasing evidence has accrued showing the effectiveness of therapeutic agents in the prevention and treatment of glucocorticoid-induced bone loss. In 1998, after several randomised controlled trials, as well as systematic reviews and meta-analyses, a UK Consensus Group synthesised the available information into guidelines for clinical practice.[21] These guidelines were summarised into a flow chart, a copy of which has been displayed in all outpatient consultation rooms of the Rheumatology Department in the Portsmouth Hospitals NHS Trust, UK, since 1998. In a recent collaborative document produced by the Royal College of Physicians, National Osteoporosis Society and Bone and Tooth Society, revised recommendations have been published[22] and it has been suggested that the management of glucocorticoid-induced osteoporosis be audited in primary and secondary care and a standardised audit tool is under development. In this study, pre-dating the new guidelines, we aimed to explore the level of adherence to the 1998 UK Consensus guidelines among a sample of outpatients treated with glucocorticoids for rheumatic diseases. Such information will establish a baseline against which future standards may be measured.

Subjects and methods

Since 1990, data have been collected annually about every patient attending a rheumatology outpatient appointment in the trust over a four-week period. For each patient, the consulting physician recorded information about demography, diagnosis(es) and current treatment, including glucocorticoids. All patients (aged >18 years) identified by the 2002 survey as current glucocorticoid-users were eligible for inclusion in this study. One observer reviewed the

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case notes of each subject according to a predefined proforma. Information was collected about type, duration and dose of glucocorticoids (maximum, minimum, cumulative and current); general preventive measures (eg smoking, calcium and vitamin D, alcohol, exercise, menopausal status); whether or not the patient had significant risk factors: ie dose of prednisolone >15 mg daily, history of a fragility fracture, age >65 years, history of maternal hip fracture, low body mass index (BMI) (<20 kg/m^2), early menopause (age <45 years)); treatments prescribed and whether or not a bone densitometry scan had been performed.

Audit standards

Based upon the 1998 UK Consensus guidelines, the following audit standards were set: 100% of adults taking glucocorticoids who were at high risk because of the presence of one or more of the following risk factors: dose of prednisolone (or equivalent) >7.5 mg for more than 6 months, age >65 years, previous fragility fracture, early untreated menopause (age <45 years) or low body mass index (<20 kg/m^2) should have been at least assessed, and if not, treated for osteoporosis.

The results were summarised by means of descriptive statistics.

Results

Over the four-week data collection period, 1,290 adults attended outpatient appointments at the Portsmouth Hospitals NHS Trust, amongst whom 189 (15%) were currently taking glucocorticoids. Between March and August 2002, the case notes of all 189 subjects were requested and 175 (93%) were available for review. The age, sex, diagnosis and steroid history for the 175 subjects are shown in Table 1. The study sample comprised more women than men (see Table 2), and the majority of subjects were receiving glucocorticoid treatment for either rheumatoid arthritis or polymyalgia rheumatica (total = 139, 79%). At the time of the study, 62 patients (35%) were receiving at least 7.5 mg of prednisolone (or equivalent) daily and the majority (91%) had been taking glucocorticoids for more than six months. The majority of patients were taking calcium (n = 110, 63%) and a sizeable minority was also taking vitamin D (n = 80, 46%).

The Consensus Group algorithm relies upon identification of those glucocorticoid users at 'high risk', as defined by a prevalent osteoporotic fracture, glucocorticoid dose ≥15 mg daily and/or age >65 years, or by the presence of other strong risk factors BMI <20 kg/m^2; maternal history of hip fracture; T score <–1.5 SD below the young adult mean at the hip or lumbar spine; or, among women, early menopausal age (<45 years)). Table 3 summarises the recording of the risk status data: glucocorticoid dose and patient's age were universally recorded but data about prevalent osteoporotic fractures were sparse. Radiographs of the thoraco-lumbar spine had been undertaken in 28 (16%) patients, amongst whom 13 had evidence of prevalent vertebral deformity. Maternal history of hip fracture and data about menopausal age were only rarely available. Sixty-eight (38.9%) patients had been sent for dual energy X-ray absorptiometry (DXA) scanning, among whom 36 had a T score <–1.5 at the hip and/or lumbar spine.

Table 1. Characteristics of the 175 study subjects.

	Men (n = 42)		Women (n = 133)	
Mean age (years)	64.2		66.9	
Diagnosis	**Number**	**(%)**	**Number**	**(%)**
Taking glucocorticoids for non-rheumatological diagnosis	3	7%	7	5%
Rheumatological diagnoses				
• Rheumatoid arthritis	13	31%	65	49%
• Polymyalgia rheumatica	19	45%	42	32%
• Connective tissue disease	5	12%	18	14%
• Other	2	5%	1	0.5%
Duration of glucocorticoids				
<1 month	2	5%	6	5%
1–6 months	2	5%	6	5%
>6 months	38	90%	121	90%
Current dose of prednisolone (or equivalent) (mg)				
<7.5 mg	22	52%	90	68%
≥7.5 mg	20	48%	42	31.5%
Unknown	0		1	0.5%
Total dose of prednisolone (or equivalent) ever (mg)				
Median	7,816.5		9,465	
Range	60 – 57,135		60 – 124,100	
Ever had DXA scan	9 (21%)		59 (44%)	

DXA = dual energy X-ray absorptiometry.

Table 2. Documentation of the general measures for the prevention and treatment of glucocorticoid-induced osteoporosis among the 175 study participants.

	Recording of information about clinical risk factors in the notes	
	Information not recorded in notes	Where documented, number with the risk factor
Lifestyle factors		
Current cigarette smoker	39	27
Taking excessive alcohol	49	5
Not taking regular exercise	167	5
Known to have had at least one fall in past 6 months	170	3
Women only (n = 133)		
Post-menopausal	16	111

Although the data were in some cases incomplete, 124 patients (71%) could be identified from the notes as at high risk, 25 as not at high risk (14%) and in the remaining 26 patients (15%) the risk status was not quantifiable because of the lack of clinical information. Table 4 summarises the treatment of the study participants stratified by assessment of risk status. In total, 76 (61%) of the 124 high-risk patients were currently receiving bone protective treatment (69 (56%) receiving bisphosphonates and seven (6%) hormone replacement therapy (HRT)), leaving 55 (39%) patients amongst whom the audit standards were not met. Among nine of these 55 high-risk patients, however, despite clear recommendations were in the notes that the patients should commence prophylaxis, no treatment had been started. In contrast, the treatment of the 68 patients in whom bone densitometry had been performed is summarised in Table 5. Among the 36 patients with a T score <–1.5, only three (8.3%) patients had not been offered prophylactic treatment.

Figure 1 represents a summary of the UK Consensus algorithm for the prevention of glucocorticoid-induced osteoporosis among this cohort of 175 patients. Where prevalent osteoporotic fractures or a T score of <–1.5 SD below the young adult mean had been documented, the majority of patients had been appropriately prescribed therapy (21/26 = 81%). In contrast however, identification of patients for therapy on the basis of clinical risk factors was generally less well performed (58/106 = 55%).

Table 3. Availability of information necessary for the Identification of 'high risk' patients according to the 1998 UK Consensus group guidelines.[20]

	Information recorded in the notes		No of individuals identified as being at 'high risk' by the presence of each risk factor
	No for whom data recorded	% of total sample (n = 175)	
Dose of prednisolone ≥15 mg/day (or equivalent)	174	99.5	10
Prevalent osteoporotic fracture			
• Distal forearm	0	0	0
• Vertebral	28	16.0	13
• Hip	0	0	0
Presence of strong risk factors			
• Age >65 years	175	100	110
• BMI <20 kg / m^2	70	40.0	0
• Maternal history of hip fracture	6	3.4	0
In women: (n=133)			
• Early menopause, (age < 45 years)	41	30.8	3
DXA scan			
• DXA scan requested	68	38.9	
• DXA result in notes	61	34.8	
T score <–1.5 **SD below the young adult mean**			36

BMI = body mass index; DXA = dual energy X-ray absorbiometry

Key Points

Prolonged oral glucocorticoid therapy is associated with accelerated bone loss and an increased risk of fracture

Rheumatologists are among those specialists most likely to report that they will offer appropriate bone prophylaxis, and indeed this study confirmed a high awareness of the risks

Despite this, only 61% of high-risk patients were receiving appropriate therapy

A better strategy for the monitoring of clinical risk factors is required

Table 4. Treatment of the 175 patients according to the 1998 UK Consensus Guidelines definition of risk status.

Patients at 'high risk'	Number	% of high-risk sample (n = 124)
Bisphosphonates – Any	69	55.6
• Alendronate (daily)	5	4.0
• Alendronate (weekly)	25	20.2
• Etidronate	36	29.0
• Risedronate	1	0.8
• Etidronate and HRT	1	0.8
• Risedronate and HRT	1	0.8
HRT	7	5.6
Patient advised but not currently taking treatment	9	7.3
Not on any treatment	39	31.5

Patients not at 'high risk'	Number	% of 'not at high risk' sample (n = 25)
Bisphosphonates	6	24.0
HRT	4	16.0
Not on any treatment	15	60.0

Risk status of patients not quantifiable due to lack of clinical information	Number	% of sample with risk status not known (n = 26)
Bisphosphonates	7	26.9
HRT	4	15.4
Calcitriol	1	3.8
Not on any treatment	14	53.8

HRT = Hormone replacement therapy.

Table 5. Bone mineral density (BMD) results and treatment of the 68 patients who had DXA scans.

	No of patients	Current treatment	No (%) of subjects receiving each treatment
T score >1.0	7	HRT	2 (29%)
		No treatment	***5 (71%)***
T score –1.5 to 1.0	18	Bisphosphonates	7 (39%)
		HRT	2 (11%)
		No treatment	***9 (50%)***
T score <–1.5	36	Bisphosphonates	25 (69%)
		HRT	3 (8%)
		Combination	1 (3%)
		Refused treatment	4 (11%)
		No treatment	***3 (8%)***

HRT = hormone replacement therapy.

Discussion

The results of this study suggest a reasonable level of awareness of the risks of glucocorticoid-induced osteoporosis among practising British rheumatologists. As a proportion of attendees at rheumatology outpatient clinics, 15% being current glucocorticoid users is conservative compared with other rheumatology surveys[19] and only 35% of the 175 patients were currently taking more than 7.5 mg prednisolone daily. Calcium supplementation was taken by 63% and vitamin D supplementation by 46%. Among those at highest risk of osteoporosis, 61% were receiving prophylaxis (among whom 69 patients (56%) were receiving bisphosphonates) and nine additional (7%) patients had been recommended treatment. Among those with evidence of prevalent fragility fracture, adherence to the guidelines was 85% (11/13 on treatment) and among those with bone mineral density evidence of osteopenia (a T score of <–1.5), adherence was 77% (10/13 on treatment). Identification and treatment on the basis of clinical risk factors was generally less consistent (58/106 = 55%) and more work is recommended in order to improve this aspect of care.

The results of this study need to be considered in the context of several limitations. The methodology of this study involved a retrospective case note review. Such a study design allowed an accurate assessment of recent current practice, without introduction of bias by influencing usual practice. However, documentation in case notes is notoriously unreliable: physicians may have performed a screen of clinical risk factors with the patient and failed to record the findings. Although every effort was made to secure the notes of all 190 patients identified as glucocorticoid users, 15 sets of notes were not available. This may have influenced the results of this study if these patients were in some way systematically different with respect to their risk of osteoporosis from the remainder. Comparison of the demographic characteristics and glucocorticoid use however suggested no important differences in terms of age, gender or diagnosis among the 15, but a marginally greater proportion (7/15) of subjects for whom notes were not available were taking ≥ 7.5 mg prednisolone daily.

Our study has highlighted the question of screening for vertebral deformity. Prevalent osteoporotic fracture is a highly significant predictor of future fracture but many vertebral fractures are subclinical. Among this cohort of steroid users, vertebral radiographs had only been requested for 28 patients. Interestingly, however, 13 of the selected 28 patients were found to have evidence of vertebral deformity, suggesting that the physicians were identifying for radiographs those at highest risk. It remains a possibility however, that a greater number of prevalent deformities would have been identified had more widespread radiographic screening been carried out.

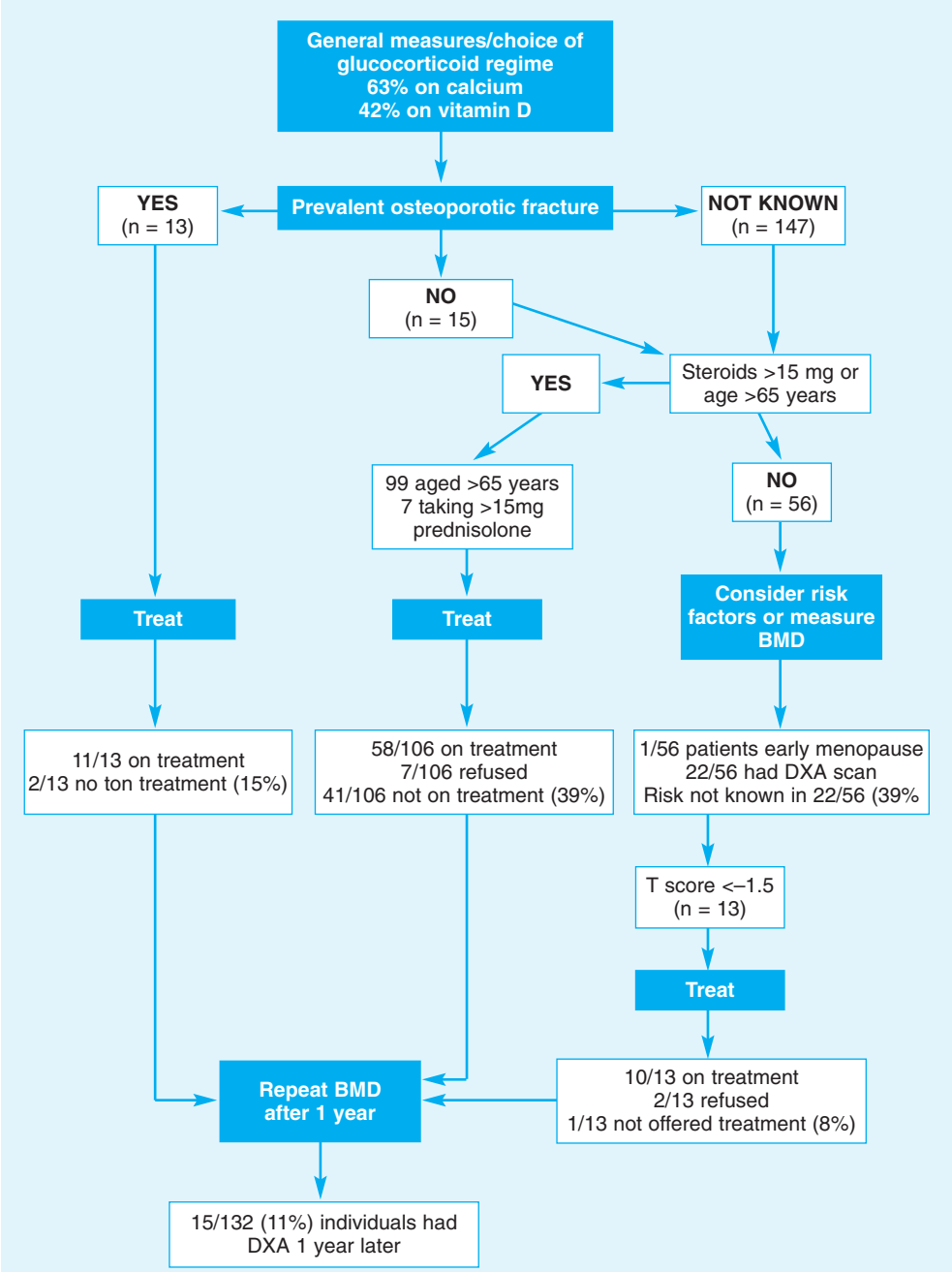

Fig 1. Summary of adherence to UK Consensus group guidelines.

Compared with the findings among glucocorticoid users in the general population,[4–5,8] ophthalmology clinics,[13] medical wards[7,11] and medical outpatient clinics,[14] the results of this study suggest that rheumatology outpatients receiving glucocorticoids were more likely to have been offered bone density measurement and/or prophylactic treatment. It appears that practising rheumatologists have a generally higher level of awareness of glucocorticoid-induced osteoporosis and are more likely to evaluate risk and consider appropriate bone-sparing therapy. This had been previously suggested by a survey of physicians' attitudes to glucocorticoid-induced osteoporosis[15] and by comparison of measures taken to prevent glucocorticoid-induced bone loss among a subset of medical inpatients in a large teaching hospital in Australia,[16] and in a regional British survey.[19] We have shown that, in the presence of reduced bone density or a prevalent osteoporotic fracture, appropriate therapy is highly likely to have been considered. In contrast however, the recording of clinical risk factors such as BMI, early age at menopause, history of maternal hip fracture is inconsistent. In the light of the recent Royal College of Physicians recommendations that mechanisms are put in place in primary and secondary care to ensure effective management of glucocorticoid-induced osteoporosis is implemented and reviewed,[22] we would recommend that attention is paid to the recording and evaluation of general measures eg nutrition, tobacco use, alcohol intake, calcium and vitamin D and clinical risk factors.

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