Improving trends in glucocorticoid-induced osteoporosis management: 2002 to 2006

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Abstract

Objective

In 2002 we undertook an audit of GIO (glucocorticoid-induced osteoporosis) management in the outpatient clinics of our university teaching hospital and found a wide variation in practice and considerable under-treatment of patients. We re-audited our practice in 2006.

Methods

A retrospective chart audit was undertaken over a 4-month period of 3,475 patients attending the 3 medical specialty outpatient clinics that were originally audited in 2002. All glucocorticoid (GC) users over the past 6 months were identified. Demographic data and treatment details were extracted, and findings were compared with the previous audit.

Results

Two hundred and fifty-three (7%) patients were identified to be taking GC vs. 104 (2%) in 2002. GIO risk was documented in 71% (179) ($p < 0.001$) of the charts vs. 13% (19) in the previous audit. In 2002, 56% (58) were on some form of bone protection [53% (55) on Ca/vitamin D and 29% (30) on a bisphosphonate] whereas in 2006 the figures were 86% (219), 82% (207) and 57% (144), respectively. DXA scanning was performed in 32% (82) of our patients in 2006. Nonetheless, considerable variation in practice was still seen, with prescription rates for anti-resorptive therapy varying from 24%-70% and those for Ca/vitamin D supplements ranging from 15%-95% for different services. For the highest risk patients, the prescription rates by specialty ranged from 36%-72% for anti-resorptive therapy and 76%-95% for Ca/vitamin D supplements.

Conclusions

Over 4 years, major improvements in GIO management have taken place in our institution, with almost a doubling of the prescription of bone protectants. However, there still remains a considerable variation in individual practices and an under-utilisation of DXA scanning. We believe that these overall, encouraging findings can be generalized to similar institutions elsewhere.

Key words

Glucocorticoid-induced osteoporosis, glucocorticoid, quality of care, treatment, audit.

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Introduction

Glucocorticoids (GC) are widely used in the treatment of many inflammatory diseases such as rheumatoid arthritis (RA), inflammatory bowel diseases and asthma, but they may contribute to and/or exacerbate osteoporosis (OP). Bone loss is demonstrable within 3 to 6 months of initiating therapy and the risk of subsequent fracture appears to be related to the dose and duration of GC therapy (1), although it has been reported with prednisolone doses as low as 2.5 mg/day. GC leads to an increased risk of fracture in 50% of patients, resulting in higher morbidity, mortality and medical expenses (2, 3). The estimated cost of all osteoporotic fractures in the US was $13.8 billion in 1995 (2, 3). There are estimated to be over 1.3 million osteoporotic fractures/year in the US (2, 3). Postmenopausal women who already have a low bone mass are likely to reach a fracture threshold with GC treatment sooner than patients with initially higher bone mineral density (BMD).

GC exert their effects on the skeleton by reducing bone formation and increasing resorption by various mechan-isms. There are GC receptors in bone cells. GC affect the differentiation and activity of osteoblast lineage cells, the transcription of many of the genes responsible for the synthesis of matrix constituents by osteoblasts (such as type 1 collagen, osteocalcin, fibronectin, alkaline phosphatase and others), and the synthesis and activity of many factors that act locally, including cytokines (interleukins 1 and 6), insulin-like growth factors (IGF-I and IGF-II), and several IGF-binding proteins (IGFBP-3, 4 and 5). Recent evidence indicates that, in addition to the decrease in osteoblastogenesis, there is an increase in the apoptosis of mature osteoblasts and osteocytes (4). GC also act on osteoclastogenesis through osteoblastic signals on the receptor activator of the nuclear factor kB ligand (RANK-L) – osteoprotegerin (OPG) axis. GC enhance RANK-L, which binds and activates RANK on the surface of the osteoclast precursor, and also inhibit OPG production with the consequent induction of osteoclastogenesis (5) and an early increase in bone resorption in GIO. This increase in bone resorption could explain the response to anti-resorptive drugs in the management of GIO. GC also induce a negative calcium balance by decreasing intestinal calcium absorption and increasing the renal excretion of calcium.

Despite the presence of guidelines for the prevention of glucocorticoid-induced osteoporosis (GIO) (6-8), numerous studies have confirmed that physicians are not sufficiently active in prescribing preventative treatment for GIO (9-14). Reasons given for this include lack of awareness, inconsistency in the published guidelines, and difficulty implementing the guidelines (15). Another factor in the modern teaching hospital is the rapid turnover of junior medical staff, which makes the implementation of consistent changes in clinical practice challenging.

Our hospital is a 650-bed tertiary referral teaching hospital. In 2002, following publication of the ACR 2001 revised recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis (GIO), we undertook an audit of GIO intervention that showed considerable under-treatment (16). In only 13% of the charts was the GIO risk documented, overall only 53% of patients taking GC were prescribed vitamin D and calcium supplements, and only 29% were prescribed anti-resorptive therapy. There was also a wide variation in practice between medical teams. Awareness of GIO and adherence to appropriate preventative treatment were clearly suboptimal, but broadly similar to comparable surveys conducted in the same period (16). After the audit, our results were presented at the hospital's Medical Grand Rounds and highlighted to different groups, but no specific hospital-wide policy on GIO intervention was introduced. However, since 2002 general awareness of osteoporosis and GIO has improved greatly both in Ireland and internationally. Meetings on the subject of osteoporosis have become more frequent, better publicized and better attended.

Therefore, we felt it would be appropriate to audit current hospital practice and

compare it to the results from 2002. We also evaluated whether the increased availability of DXA scanning in our hospital had impacted on clinical practice.

Methods

From October 2005 to April 2006, chart reviews were conducted on all patients attending randomly selected general outpatient clinics in three medical specialties (rheumatology, gastroenterology and respiratory medicine), in a manner identical to the original audit conducted in 2002 (one specialty that had been audited in 2002 – Nephrology – was not re-audited due to a major change in clinical practice which effectively meant that a cohort of renal transplant patients taking GC that was comparable to the 2002 audit was not available in 2006). The three specialties audited were randomly labeled A, B and C. The purpose was to identify all patients who had been prescribed GC in the previous 6 months. The three specialty clinics were all supervised by the same lead attending (consultant) physicians in both of the audit years, with a similar mix of junior and more senior doctors-in-training attending at both time periods.

The same criteria were adopted to identify GC users as those used in 2002: patients taking prednisolone ≥ 5 mg/day for more than one year; prednisolone ≥ 7.5 mg or ≥ 10 mg/day for > 3 months or patients receiving ≥ 2 pulse courses of GC in a six-month period (20 mg prednisolone equivalent or more for > 2 weeks). Patients were assigned to one of the above groups exclusively on the basis of the highest dose of GC used in last 6 months. Those patients taking ≥ 7.5 mg or ≥ 10 mg/day of prednisolone and all women ≥ 55 years were regarded as high risk patient groups. As the audit 2006 was based on chart reviews, reliable data on menopausal status was not available; thus, all women ≥ 55 years of age were considered to be postmenopausal [a literature search shows that 95% of women become menopausal between the ages of 45 to 55 years (17)].

The following demographic data were recorded on all identified GC users: age, gender, menopausal status (women ≥ 55 years of age were considered as postmenopausal), indications for GC therapy, the medical specialty attended, and the date of attendance. The following risk factors for OP were recorded: smoking status, body weight, alcohol intake, a previous history of fracture, and a family history of fracture.

Charts were reviewed to assess whether GIO risk was mentioned when GC therapy was started. All medications prescribed for OP were recorded (Ca/vitamin D supplements, bisphosphonates, hormone replacement therapy (HRT), raloxifene, parathyroid hormone, etc.) along with most recent creatinine, electrolyte and bone biochemistry results.

The data were compared with the results for the same three specialties from the previous audit. Statistical significance was determined by Student's *t*-test and the chi-square test using the program SPSS 12.0.1 for Windows (18). Before employing the *t*-test, we checked the variances of the two groups using the Levene test of variances to make sure that the two groups were homogenous (18).

Results

Patients

In total, 3475 charts were reviewed and 253 patients (7%) were identified as taking GC. These figures were 4350 and 104 (2%) in 2002. The number of patients attending the different specialties was: A – 1330, B – 1249, and C – 896. In 2006 there were 155 (61%) female patients, of whom 100 (65%) were over 55 years of age.

Common indications for GC therapy

Table I compares the common indications for GC therapy between the two audits. The main difference was that more RA patients were identified as being on GC therapy in 2006 ($p < 0.005$). RA (32%) was the most common indication for GC therapy, while chronic obstructive pulmonary disease (COPD) and giant cell arteritis/polymyalgia were second most common (12%). In 2002 COPD/asthma (17%) and RA (17%) were the commonest indications. The difference between the audits was statistically significant only for RA ($p < 0.005$). There was little difference in terms of the percentage of patients on different doses of GC in the two audits, as shown in Table II.

Documentation of GIO awareness

In 2006, GIO risk was documented in 71% (179) of the charts vs. 13% (19) of the charts in 2002 ($p < 0.001$). GIO risk was documented in almost 100% of the patients attending the specialty B clinic compared to 0% in 2002. In 2006, GIO risk was documented in 70% of the patients attending specialty A, and 58% of the patients attending specialty C,

Table I. Common indications for GC therapy.

Indications	Audit 2006 n = 253 (%)	Audit 2002 n =151 (%)†
Rheumatoid arthritis/Sjögren's syndrome*	80 (32%)*	25 (17%)
COPD/Asthma	39 (15%)	26 (17%)
GCA/PMR/Vasculitis	36 (14%)	23 (15%)
Ulcerative colitis/Crohn's disease	28 (11%)	12 (8%)
Sarcoidosis	20 (8%)	5 (3%)
Systemic lupus erythematosus	14 (6%)	4 (2%)
MCTD/Raynaud's phenomenon	9 (4%)	2 (1%)
Autoimmune hepatitis	8 (3%)	5 (3%)
Renal transplant patients#	Not included	47 (31%)
Miscellaneous§	19 (7%)	2 (1%)

*$p < 0.001$; all other values not significant.

†After excluding renal patients from the 2002 audit, the adjusted number of patients included in the statistical analysis was 104.

#Nephrology was not re-audited in 2006 due to a major change in clinical practice which effectively meant that a cohort of renal transplant patients taking GC comparable to the 2002 audit was not available.

§Includes psoriasis, ankylosing spondylitis, ITP, undifferentiated arthritis, polymyositis, dermatomyositis, idiopathic pulmonary fibrosis, myasthenia gravis, cystic fibrosis and pan-hypopituitarism.

Table II. Percentage of patients on different doses of steroids between the two audits.

Glucocorticoid dose	2006	2002
5 mg prednisolone for over 1 year	45%	45%
7.5 mg prednisolone	9%	14%
10 mg prednisolone	26%	22%
≥ 2 courses of steroids, as outlined in the Methods section	21%	18%

compared to 29% in specialty A and 16% in specialty C in 2002.

Treatment of GIO

Patients were considered to be receiving bone protection if they were treated with any combination of calcium and vitamin D, a bisphosphonate, HRT/raloxifene (SERM), and/or teriparatide. In 2006, 86% (219) of the patients were prescribed some form of bone protection compared to 56% (58) in 2002 ($p < 0.005$). In 2006, 82% (207) of the patients received Ca/vitamin D compared to 53% (55) in 2002 ($p < 0.005$), and 57% (144) received anti-resorptive therapy compared to 29% (30) in 2002 ($p < 0.005$). Table III details these findings and also reviews the results by individual medical service. Of note, the improvement in treatment was limited to two of the specialties with no improvement noted in the third. Differences in the prescription of bisphosphonates in 2006 observed between specialties A and B in part relate to differences in recommendations between the UK Consensus Group on Osteoporosis, the Belgian Bone Club, and ACR recommendations for GIO intervention (6-8).

High risk group

All patients taking ≥ 7.5 mg/day of prednisone and all women ≥ 55 years were classified as high risk patients. Table IV compares the high risk patient groups in the two audits. The percentage of high risk patients in the two audits was the same, *i.e.* 62%. In 2006, a much higher percentage of these patients were prescribed bone protection against GIO; 87% (136) received Ca/vitamin D ($p < 0.005$) and 64% (100) received anti-resorptive therapy ($p < 0.005$), compared to 55% (35) and 44% (28) respectively in 2002.

While women ≥ 55 yrs of age are considered to be at high risk for glucocorticoid-induced osteoporosis (GIO) and were included in this group, we decided to analyze GIO intervention in women ≥ 55 separately as well, as they clearly constitute a subgroup that can be managed differently.

Major improvement was seen in terms of GIO intervention in women ≥ 55 years of age. In 2006, among 100 postmenopausal women the GIO risk was documented in 81 (81%) ($p < 0.001$); 78 (78%) were prescribed Ca/vitamin D ($p < 0.001$) and 76 (76%) received a bisphosphonate ($p < 0.005$). In contrast, in 2002 among 43 postmenopausal women, the GIO risk was documented in 21% (9), 21% (9) were on Ca/vitamin D, and 40% (17) received bisphosphonate treatment. Improvements were seen in all specialties, but once again considerable variation was noted between specialties.

DXA scanning

A DXA scan was performed in 82 (32%) patients and 37 (15%) were diagnosed with OP. There was considerable variation the requests for a DXA scan between specialties. Over 70% of the patients in specialty B received a DXA scan, 22% in specialty A, and 18% in specialty C. DXA scanning was performed in a higher percentage of the patients attending specialty B clinics, which again partly reflects the adherence to different published guidelines for GIO intervention (6-8).

Overall, GIO intervention was more common in women than in men (80% *vs.* 40%, $p < 0.001$), with women ≥ 55 years of age receiving GIO intervention more frequently than younger women (90% *vs.* 45%, $p < 0.001$). In addition, patients 50–64 years of age were more likely to have received GIO intervention than those who were either younger or older (85% *vs.* 50%, $p < 0.005$). Patients with a longer duration of RA and inflammatory bowel disease (IBD) had a tendency toward more frequent GIO intervention than patients with MCTD (70% RA, 54% IBD, and 44% MCTD patients), while only 25% of patients with COPD received GIO management. Patients with a prior fracture or a diagnosis of OP were much more likely to have received intervention ($p < 0.001$); all 37 patients diagnosed with OP, and 12 patients with a history of fracture were on anti-resorptive therapy.

Discussion

The results of this audit show that over the 4-year period between 2002 and 2006, major improvements in GIO documentation and treatment have taken place in our institution, with nearly

Table III. Prescription of bone-sparing therapy by specialty and agent in two audits.

	Total no. on GC therapy		ANY bone protection (%)		Calcium/vitamin D (%)		Anti-resorptive therapy (%)	
	Audit 2006	Audit 2002	Audit 2006	Audit 2002	Audit 2006	Audit 2002	Audit 2006	Audit 2002
Total	253	104	219 (86%)**	58 (56%)	207 (82%)**	55 (53%)	144 (57%)**	30 (29%)
Specialty A	142	49	128 (90%)	34 (69%)	123 (87%)	29 (59%)	98 (69%)	24 (49%)
Specialty B	46	20	43 (93%)	11 (55%)	44 (95%)	11 (55%)	11 24%)	1 (5%)
Specialty C	65	35	39 (60%)	22 (63%)	10 (15%)	13 (37%)	29 (45%)	17 (49%)

** $p < 0.005$ *vs.* 2002.

Table IV. Percentage of high risk patients on bone protection.

	No. of high risk patients		No. of patients on calcium/vitamin D		No. of patients on anti-resorptive therapy	
	Audit 2006 GC users = 253	Audit 2002 GC users = 104	Audit 2006	Audit 2002	Audit 2006	Audit 2002
Total	157 (62%)	64 (62%)	136 (87%)**	35 (55%)	100 (64%)**	28 (44%)
Specialty A	98 (69%)	31 (64%)	87 (89%)	18 (58%)	71 (72%)	14 (45%)
Specialty B	22 (48%)	6 (37%)	21 (95%)	5 (83%)	8 (36%)	0 0
Specialty C	37 (56%)	27 (73%)	28 (76%)	12 (44%)	21 (57%)	14 (52%)

**$p < 0.005$ *vs*. 2002.

a doubling of prescriptions for bone protectants.

Overall, the two audits are comparable. Both were conducted in the same institution; used the same criteria to identify GC users, examined the same medical specialties, and screened approximately similar numbers of patients. However, there were some subtle differences between the two audits. More RA patients were included in the 2006 audit and this difference was statistically significant ($p < 0.005$). Nonetheless, equal percentage of RA patients (*i.e*. 70%) received GIO intervention in the 2 audits, which means that the overall change in GIO intervention came entirely from non-RA patients. This group aside, the patients were broadly similar, and the composition of the medical teams was unchanged.

There were marked differences in terms of the results in the two audits; in 2006, GIO risk was documented in 71% (179) of the patients *vs*. 13% (19) in 2002 ($p < 0.001$), and 86% (218) received some bone protection in 2006 *vs*. 56% (58) in 2002 ($p < 0.005$). In terms of the high risk patient group, in 2006 87% (136) received Ca/vitamin D, and 64% (100) received anti-resorptive therapy, compared to 55% (35) and 44% (28) respectively in 2002 ($p < 0.005$). Several patient factors were associated with the likelihood of GIO intervention, including older age, female sex, a prior fracture or diagnosis of OP, and larger doses of GC. These variables have also predicted GIO intervention in prior studies (19).

Considerable variations in individual practice were still seen in 2006. Major improvement in treatment came from two of the specialties, with no improvement noted in the third. There were also differences in the prescription of bisphosphonates in 2006 between specialties A and B, reflecting their adherence to different guidelines (6-8). The UK Osteoporosis Consensus Group (6), and the Belgian Bone Club consensus document (7) recommend GIO intervention in cases of a daily prednisolone dose ≥ 7.5 mg for ≥ 6 months, and for ≥ 3 months respectively, while the ACR (8) recommends anti-resorptive therapy at commencement of GC therapy involving ≥ 5 mg/day of prednisolone for ≥ 3 months. The harmonization of published guidelines could improve clinical practice (15).

Initial studies in the 1990s showed poor levels of treatment of GIO (20). For example, in 1997 following publication of the UK Consensus Group recommendations, Reid reported that only 8-14% of long-term GC users received some form of bone protection (21). Saag showed that between 1997 and 2001 the rates of use of bone protection in women aged over 65 improved from 24% to 44%, with smaller improvements in young women and men, but overall still low rates of GIO protection (22). Guzman showed that only 32% of patients on long-term GC therapy in 2001-2002 in the VA Greater Los Angeles Healthcare System received bone protection (9). As our audits show, in 2002 56% (58) of our patients received some bone protection (mostly in the form of bisphosphonates), in keeping with the best practice at the time, and this figure rose to 86% in 2006 ($p < 0.005$).

In a review of data from the US, Saag showed a doubling of the rates of DXA scanning (from 10% in 1996 to 19% in 2001) among post-menopausal women (22). Our 2006 audit shows that DXA scanning was performed in 32% (82) of long-term GC users. DXA scanning is still under-utilized, but this has not been an impediment to the empirical treatment of GIO. The guidelines for the use of DXA in decisions regarding treatment and its monitoring are not precise and clearer recommendations on the appropriate use of DXA scanning might improve treatment (23).

In conclusion, over the past 4 years major improvement in the documentation and treatment of GIO has taken place in our institution, with better awareness and almost a doubling of the prescription of bone protectants. However, there still remains considerable variation in individual practice, due in part to adherence to different guidelines for GIO management and in part to the under-utilisation of DXA scanning. We believe these encouraging findings can be generalized to similar institutions elsewhere.

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