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ORIGINAL ARTICLE

Glucocorticoid-induced osteoporosis preventive care in rheumatology patients

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Abstract

Summary Glucocorticoid-induced osteoporosis (GIOP) is common in patients prescribed with long-term glucocorticoids. Guidelines suggest patients receiving moderate-dose glucocorticoid therapy receive GIOP preventive care. Previous studies have shown preventive care rates are not optimal. We look at GIOP preventive care rates in rheumatology patients and predictors of various components of care.

Purpose Glucocorticoid-induced osteoporosis (GIOP) is a common concern in patients prescribed with long-term glucocorticoids. Studies have shown GIOP preventive care is not provided optimally in the general population; however, little is published on GIOP preventive care among patients with rheumatic disease. The objective of this study is to determine the proportion of rheumatology patients who received GIOP preventive care.

Methods A population-based retrospective quality assurance study of adults seen at the University of Alberta Rheumatology Clinic was performed using the electronic outpatient medical record. Records of adult patients prescribed with prednisone from January 1st to December 31st, 2016 by a rheumatologist were initially included for review. Those who had been prescribed ≥ 7.5 mg/day for ≥ 3 months were assessed for concurrent GIOP preventive care.

Results A total of 745 discreet courses of prednisone were prescribed in 433 patients with 113 meeting the above inclusion criteria. Following the prednisone prescription, 79% were taking vitamin D, 86% were taking calcium, and 50% were prescribed with osteoporosis pharmacotherapy. Twenty-five percent of patients had DXA imaging ordered by the rheumatologist within the first 6 months; of these, 86% of patients completed the DXA.

Conclusions Overall, our study shows that patients under the care of rheumatologists receive better GIOP preventative care than previously reported care in the general population. However, there is still room for improvement. In particular, men, younger patients, and rural patients seem to be at the most at risk of not receiving optimal GIOP prevention.

Keywords Glucocorticoid · Steroid · Bisphosphonate · Osteoporosis · Rheumatologist

Introduction

Systemic glucocorticoid therapy is commonly used in the management of rheumatologic diseases. While the evolving utilization of biologics to control inflammation has reduced need for their usage, glucocorticoids still remain an important therapy in the rheumatologist's toolkit despite their many known side effects [1–3]. A common, yet manageable, adverse effect is glucocorticoid-induced osteoporosis (GIOP), with previous studies reporting fractures in 30 to 50% of patients receiving long-term glucocorticoid therapy [4]. Within the first year of starting systemic glucocorticoids, 6 to 12% of bone mineral density (BMD) is lost, with 3% per year lost thereafter [5]. Risk of fracture increases by as much as 75%

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within the first 3 months of therapy, even before notable decreases in BMD, which implies adverse effects on bone physiology not captured by densitometry alone [6, 7]. Osteoporotic fractures significantly contribute to functional loss, morbidity, mortality, and health-related costs in affected patients [8–10].

Fortunately, there are proven treatments recommended by current regional guidelines (Osteoporosis Canada 2010) which reduce morbidity associated with GIOP [11]. All patients should receive adequate calcium and vitamin D supplementation, but these precautions alone are not sufficient to prevent fractures [11, 12]. Bisphosphonates are considered to be the first-line option for the treatment and prevention of glucocorticoid-induced osteoporosis but other medications including denosumab and teriparatide have also been shown to be effective [11]. BMD testing is generally recommended within first 6 months of starting moderate- to high-dose systemic glucocorticoids [4, 11, 13].

Administrative databases have shown GIOP preventative care is not optimal in the general population. Estimates suggest only 22–36% of patients are started on appropriate pharmacotherapy and 6–8% undergo BMD testing [14, 15]. However, little is known about GIOP preventive care among patients specifically under the care of rheumatologists. Subgroup analyses in administrative database studies of the general population have suggested patients under the care of rheumatologists receive better GIOP preventive care compared to other specialties, but there are few studies specifically designed to assess for this [15, 16].

The objective of this study is to determine the proportion of general rheumatology patients seen at the University of Alberta in 2016 who received recommended GIOP preventive care, as outlined by the Osteoporosis Canada 2010 guidelines, including calcium and vitamin D supplementation, preventative pharmacotherapy, and BMD study within 6 months of newly starting moderate to high doses of long-term prednisone (greater than or equal to 7.5 mg/day for 3 months, as defined by Osteoporosis Canada 2010 guidelines), depending on patient age [11]. Our secondary objective is to determine independent patient characteristics which are predictors of individual components of GIOP preventive care.

Methods

A formal ethics application based on the study protocol was submitted to the University of Alberta Research Ethics Office. Given the nature of our study (quality assurance), ethics approval was granted without formal board review.

Using the electronic medical record "eClinician," a database query was performed to identify records of all adults over 18 years of age newly prescribed a course of prednisone from January 1st to December 31st, 2016 by a rheumatologist working at the University of Alberta Hospital (14 in total). Prednisone prescriptions were reviewed and the average daily prednisone dose within the first 3 months of prescription was calculated. Patients who were prescribed greater than or equal to 7.5 mg per day for greater than or equal to 3 months were included in this study. Patients with established osteoporosis, pre-existing osteoporosis pharmacotherapy, previous fragility fracture, or a previous BMD study within 1 year prior to starting prednisone were excluded. A retrospective manual chart review was performed for the various aspects of GIOP preventive care, including patient-reported intake of calcium and vitamin D supplementation, ordering of GIOP preventive pharmacotherapy, ordering of BMD, and completion of BMD. Medications that were deemed appropriate for GIOP prevention included alendronate, risedronate, zoledronic acid, denosumab, raloxifene, and teriparatide [13].

We calculated crude incidence rates for the above components of GIOP preventive care for all patients as well as for sub-groups in patients less than 50 years of age and greater than or equal to 50 years of age. For patients less than 50 years of age, we defined composite GIOP preventive care as self-reported vitamin D supplementation and completion of BMD study within 6 months of prednisone prescription. For patients greater than or equal to 50 years of age, we defined composite GIOP preventive care as self-reported vitamin D supplementation, prescription of pharmacotherapy, and completion of BMD study within 6 months of prednisone prescription. This framework was based on the suggestions of our regional guidelines [11]. Our study did not assess for levels of dietary calcium intake; thus, calcium supplementation was not included as a component of GIOP composite preventive care, as patients who receive adequate dietary calcium do not require supplementation. We analyzed variables of interest according to whether or not each individual component of GIOP prevention was fulfilled using multivariate regression. SPSS (IBM Corp. Released 2018. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used for all analyses.

Results

A total of 745 discreet courses of glucocorticoids were prescribed in 433 discrete patients (Fig. 1) by rheumatologists in the outpatient setting at the University of Alberta from January 1st to December 31st, 2016. Of these, 305 patients met the inclusion criteria (average prednisone dose ≥ 7.5 mg/day for ≥ 3 months). One hundred ninety-two patients were excluded based on criteria listed above, leaving 113 patients. Baseline demographic information was collected (Table 1).

Following initiation of prednisone, 50% (56/113) were prescribed GIOP pharmacotherapy. Bisphosphonates were prescribed to all 56 patients, with no prescription of denosumab, raloxifene, or teriparatide. Forty-five patients

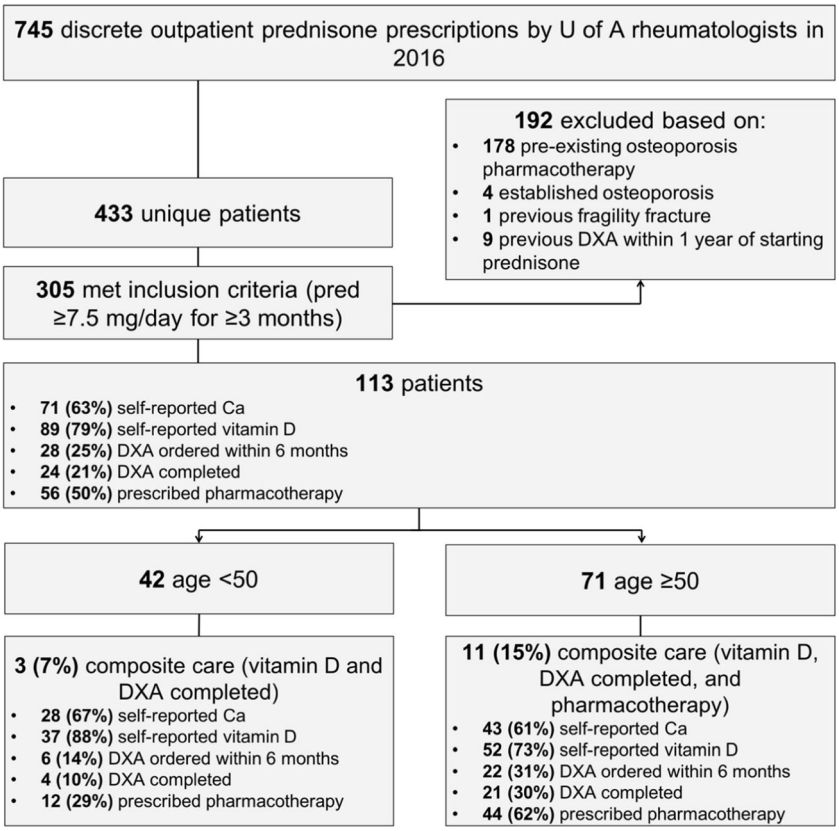

Fig. 1 Study participant inclusion/exclusion flow chart and GIOP preventive care treatment distribution

were prescribed alendronate; nine patients, risedronate; and two patients, etidronate. Twenty-five percent (28/113) of the patients had a BMD study ordered within the first 6 months, with 57% (64/113) having at least one of these two components of GIOP prevention ordered (Fig. 1). Seventy-nine percent (89/113) were taking vitamin D supplementation and 63% (71/113) were taking calcium supplementation within 6 months of starting prednisone. Eighty-six percent (24/28) of ordered BMDs were completed.

For patients less than 50 years of age, following initiation of prednisone, 29% (12/42) were prescribed with GIOP pharmacotherapy. Fourteen percent (6/42) of patients had a BMD study ordered within the first 6 months, and 10% (4/42) completed the study. Eighty-eight percent (37/42) were taking vitamin D supplementation and 67% (28/42) were taking calcium supplementation within 6 months of starting prednisone. Seven percent (3/42) completed BMD study and were taking vitamin D supplementation within 6 months, as recommended by our regional guidelines [11].

For patients greater than or equal to 50 years of age, following initiation of prednisone, 62% (44/71) were prescribed with GIOP pharmacotherapy. Thirty-one percent (22/71) of patients had a BMD study ordered within the first 6 months, and 30% (21/71) completed the study. Seventy-three percent (52/71) were taking vitamin D supplementation and 61% (43/71) were taking calcium supplementation within 6 months of starting prednisone. Fifteen percent (11/71), who completed BMD study, were taking vitamin D supplementation within 6 months, and were prescribed GIOP pharmacotherapy as is recommended by our regional guidelines [11].

The following independent variables were included for multivariate analysis: gender, age, glucocorticoid starting dose, average glucocorticoid dose over the first 3 months, glomerular filtration rate (GFR), and geographic location (urban vs rural). Rural location was defined using Canada Post criteria [17]. Female gender was associated with a higher likelihood of having a BMD study ordered (OR = 2.80 [95% C.I. = 1.03–7.63]) and self-reported vitamin D supplementation (OR = 2.78 [95% C.I. = 1.06–7.28]) (Table 2). Age greater than or equal to 50 increased the likelihood of receiving a prescription for GIOP pharmacotherapy (OR = 4.56 [95% C.I. = 1.76–11.84]). Higher starting prednisone dose was correlated with increased GIOP pharmacotherapy (OR = 1.15 [95% C.I. = 1.05–1.26]). However, higher average prednisone doses over the first 3 months were negatively correlated with GIOP pharmacotherapy (OR = 0.888 [95% C.I. = 0.805–0.980]). Rural residence was negatively correlated with GIOP pharmacotherapy (OR = 0.10 [95% C.I. = 0.0.025–0.403]), DXA ordering (OR = 0.21 [95% C.I. = 0.043–0.971]).

Table 1 Baseline characteristics of all patients included in the final analysis, sub-grouped based on various components of GIOP preventive care

	All patients ($n = 113$)	Calcium			Vitamin D			Pharmacotherapy			Dual-energy X-ray absorptiometry		
		Taken ($n = 71$)	Not taken ($n = 42$)	p	Taken ($n = 89$)	Not taken ($n = 24$)	p	Prescribed ($n = 56$)	Not prescribed ($n = 57$)	p	Ordered ($n = 28$)	Not ordered ($n = 85$)	p
Age													
≥ 50	71	43	28	0.516	52	19	0.061	19	27	0.147	18	53	0.857
< 50	42	28	14	0.516	37	5	0.061	37	30	0.147	10	32	0.857
Female	69	44	25	0.795	59	10	0.028	33	36	0.646	21	48	0.082
Urban	90	60	30	0.095	73	17	0.226	52	38	0.001	26	64	0.046
Diagnostic category													
Connective tissue disease	25	16	9	0.889	21	4	0.465	6	19	0.004	6	19	0.920
Vasculitis	32	18	14	0.363	26	6	0.681	22	10	0.010	11	21	0.136
Inflammatory arthritis	15	5	10	0.011	9	6	0.056	5	10	0.177	1	14	0.082
Myositis	8	7	1	0.134	8	0	0.128	5	3	0.447	2	6	0.984
Other	33	25	8	0.067	25	8	0.617	18	15	0.497	8	25	0.936
Mean starting prednisone dose (mg/day)	27.3	27.2	27.6	0.901	27.8	25.5	0.550	31.5	23.3	0.006	27.6	27.3	0.934
Mean average prednisone dose in first 3 months (mg/day)	23.1	22.2	24.6	0.418	23.3	22.2	0.756	25.6	20.6	0.066	24.3	22.7	0.629
Mean glomerular filtration rate (mL/min)	82.6	83.1	81.7	0.824	84.2	76.5	0.324	81.3	83.8	0.697	88.8	80.5	0.18
Mean number concurrent medications	9.7	9.5	9.9	0.679	9.9	8.8	0.279	10.6	8.8	0.044	9.9	9.6	0.755
Mean number comorbidities	4.4	4.5	4.3	0.768	4.6	3.8	0.189	4.6	4.3	0.665	4.3	4.4	0.883

Table 2 Odds ratios (OR) for selected independent variables in predicting GIOP preventive care calculated via multivariate logistic regression

	Vitamin D		Calcium		Pharmacotherapy		DXA ordered		DXA completed	
	OR (95% C.I.)	*p*	OR (95% C.I.)	*p*	OR (95% C.I.)	*p*	OR (95% C.I.)	*p*	OR (95% C.I.)	*p*
Female	2.777 (1.060–7.281)	0.038	1.140 (0.504–2.582)	0.753	1.025 (0.410–2.559)	0.958	2.801 (1.029–7.626)	0.044	2.589 (0.904–7.417)	0.077
Age ≥ 50	0.326 (0.103–1.033)	0.057	0.729 (0.312–1.702)	0.465	4.564 (1.759–11.844)	0.002	1.117 (0.433–2.884)	0.819	0.990 (0.371–2.646)	0.984
Starting prednisone dose (continuous)	1.047 (0.959–1.143)	0.303	1.072 (0.992–1.159)	0.078	1.149 (1.045–1.263)	0.004	0.957 (0.877–1.044)	0.323	0.971 (0.890–1.060)	0.511
Average prednisone dose in first 3 months (continuous)	0.964 (0.876–1.060)	0.449	0.921 (0.847–1.001)	0.053	0.888 (0.805–0.980)	0.018	1.054 (0.959–1.158)	0.276	1.044 (0.950–1.147)	0.373
Glomerular filtration rate < 30 mL/min	1.011 (0.067–15.303)	0.994	0.594 (0.073–4.819)	0.626	0.214 (0.012–3.721)	0.290	0.0 (0–0)	0.999	0 (0–0)	0.999
Rural residence	0.385 (0.124–1.199)	0.100	0.408 (0.155–1.079)	0.071	0.101 (0.025–0.403)	< 0.001	0.205 (0.043–0.971)	0.046	0.089 (0.054–1.231)	0.089

Discussion

Previous studies have demonstrated sub-optimal osteoporosis treatment even in patients who qualify for GIOP preventative care based on treatment guidelines [18]. However, there are no reported studies specifically examining GIOP preventative care rates in the general rheumatology patient population [15, 19]. Our study shows suboptimal adherence (15% following vitamin D, DXA scan, and pharmacotherapy recommendations) to GIOP preventative care according to Osteoporosis Canada 2010 practice guidelines in patients managed by rheumatologists [11].

However, rheumatologists at our center appear to have a higher prescribing rate of GIOP preventative care as compared to prescription fill rates seen in the general population that is reported from administrative database studies (50% prescription rate for pharmacotherapy in our study compared to 12–22%) [14, 15]. This may reflect better implementation of GIOP prevention measures by rheumatologists or a major gap between prescribing and fill rates. A previous systematic review on the prevalence of GIOP management reported that in most studies, less than 40% of chronic oral glucocorticoid users received BMD testing or osteoporosis treatment [16]. Trijau et al. did report a higher rate of GIOP preventive care if the initial glucocorticoid prescriber was a rheumatologist (65% prescription rate in rheumatologists vs 12% in primary care), with an odds ratio of between 2.5 and 3.0 for the various aspects of GIOP prevention [15]. Another study by Watt et al. reported that 47% of patients with RA using corticosteroids ≥ 7.5 mg/day for ≥ 3 months were prescribed a bisphosphonate, comparable to the 50% bisphosphonate prescription rate in our study [20].

Our study certainly shows a discrepancy between DXA scans being ordered and completed, with 86% of DXA scans ordered for GIOP preventative care actually being completed. This discrepancy has not been reported before in this population since administrative databases only capture completed DXA scans.

Higher rates of calcium (63%) and vitamin D (79%) supplementation compared to the general population taking glucocorticoids (less than 18% for both) were seen in our cohort. Since most calcium and vitamin D supplementation is not prescribed, administrative databases are likely underreporting the true rate of calcium and vitamin D supplementation. The nurses at the University of Alberta rheumatology clinic review all prescription and over-the-counter medications (including supplements and natural health products) at each patient visit, perhaps allowing a more accurate rate of use among our patients.

We found multiple patient demographic factors to be statistically significant predictors of GIOP preventive care in our statistical models. Previous studies have reported age, sex, and provider specialty as important predictors in GIOP

management, and our results echo this [15, 16]. Unsurprisingly, female gender was associated with increased rates of BMD study ordering (OR = 2.80 [95% C.I. = 1.03–7.63]). This likely reflects current osteoporosis screening guidelines due to known increased risk of osteoporosis in post-menopausal women [21–23]. In addition, age greater than or equal to 50 was correlated with increased prescription of GIOP pharmacotherapy (OR = 4.56 [95% C.I. = 1.76–11.84]). Age is a widely known risk factor for osteoporosis and fragility fracture, likely playing an important role in clinical practice patterns [13, 22].

Higher glucocorticoid starting doses were associated with increased rates of GIOP pharmacotherapy prescription (OR = 1.15 [95% C.I. = 1.05–1.26]). However, interestingly, increased average daily dose (all greater than or equal to 7.5 mg/day), which is the more important factor, was negatively associated with GIOP pharmacotherapy prescription rates (OR = 0.888 [95% C.I. = 0.805–0.980]). This may be because patients with higher average glucocorticoid doses may have an overall larger burden of acute and chronic disease with multiple complications and comorbidities, and so the clinician may be focused on other aspects of the patient's care.

We also found that rural residence was associated with decreased rates of GIOP pharmacotherapy (OR = 0.10 [95% C.I. = 0.025–0.403]), as well as DXA ordering (OR = 0.21 [95% C.I. = 0.043–0.971]). Rural patients may have increased barriers when accessing healthcare, which may affect rates of GIOP preventative care.

Results from previous studies have similarly demonstrated female sex, older age, and urban residence to be strong predictors of osteoporosis screening and therapy, and our results specifically in the GIOP general rheumatology population correlate well with this [19, 20]. However, our findings regarding glucocorticoid starting and average doses as predictors of GIOP preventative care have not been previously described.

This is the first study, to our knowledge, to specifically report GIOP preventive care rates in the rheumatology patient population. This study differs from previous studies on GIOP prevention in that a chart review was completed on each patient as compared to administrative data which have their own set of limitations. As well, we were able to examine physician ordering rates of pharmacotherapy and DXA scans, whereas previous studies only examined the pharmacotherapy fill rate and DXA scan completion rate. This allows us to address the gap in care at the physician level. Our sample size (n = 113) was smaller than prior administrative database studies of the general population. However, we were still able to demonstrate similar trends to previous studies.

Overall, this study shows that patients under the care of rheumatologists receive suboptimal GIOP preventative care. Men, younger patients, patients on higher average doses of prednisone, and rural patients seem to be at the most risk of not receiving optimal GIOP prevention. Interventions need to be developed to address this care gap at the physician level, and further studies looking at patient adherence and persistence with GIOP preventive care are needed.

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Compliance with ethical standards

Conflicts of interest None.

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