Use of a Computerized Order Set to Increase Prescription of Calcium and Vitamin D Supplementation in Patients Receiving Glucocorticoids

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BACKGROUND: American College of Rheumatology guidelines recommend that patients taking glucocorticoids also take calcium and vitamin D supplements, regardless of the dose or intended duration of glucocorticoid use, to decrease their risk of glucocorticoid-induced osteopenia or osteoporosis (GIOP).

OBJECTIVE: To increase the number of prescriptions made for calcium and vitamin D in patients who receive a prescription for glucocorticoids using an automated, computerized order set.

DESIGN: Pre-post test design.

PATIENTS: A total of 1,041 outpatients receiving care at a single VA medical center.

INTERVENTION/MAIN MEASURES: We developed an automated order set in which calcium and vitamin D were automatically co-ordered with glucocorticoid prescriptions of at least 2-week duration. We tested the impact of the order set by comparing the number of calcium and vitamin D prescriptions in patients taking glucocorticoids during a 12-month period before (T1) and after (T2) implementation. The automated order set could be modified by the treating physician, and it was not generated for patients with hypercalcemia.

KEY RESULTS: A total of 535 patients during T1 and 506 patients during T2 had a glucocorticoid prescription of at least 2-week duration. The percent of co-prescriptions for calcium increased from 37 to 49 % and vitamin D from 38 to 53 % (both $p<0.0001$) after the new automated order set was implemented.

CONCLUSIONS: Implementation of an automatic prescription for calcium and vitamin D supplementation modestly increases the number of patients on glucocorticoids who are prescribed calcium and vitamin D supplementation.

KEY WORDS: glucocorticoid-induced osteoporosis; adherence; calcium; vitamin D; prednisone.

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INTRODUCTION

Glucocorticoids are associated with significant bone loss and osteoporotic fractures. Bone loss begins early, and the increase in fractures is seen with the first year of therapy. Glucocorticoid-induced osteoporosis (GIOP) can be managed using calcium and vitamin D supplementation as well as bisphosphonates. The American College of Rheumatology guidelines recommend that all patients (both men and women) taking glucocorticoids use calcium and vitamin D supplements, regardless of their risk profile, glucocorticoid dose or intended duration of use.[1] These recommendations are based on the safety profile of moderately dosed calcium and vitamin D and studies demonstrating that (1) oral glucocorticoids can lead to rapid bone loss within the first 3 months of glucocorticoid use,[2] and (2) while the risk of GIOP increases with the cumulative glucocorticoid dose, there is no dose of glucocorticoids that does not accelerate bone loss or increase fracture risk;[3,4] (3) several randomized controlled trials have shown that the administration of calcium and vitamin D in patients undergoing glucocorticoid therapy can prevent early bone loss.[5–7] In contrast, recommendations regarding the use of bisphosphonates are individualized based on risk factors and childbearing potential.

Despite the impact of GIOP, studies have shown that there is poor adherence with calcium and vitamin D supplementation as well as bisphosphonate use.[8–11] While decision-making related to bisphosphonates involves difficult trade-offs among the potential benefits, known toxicity and unknown long-term effects, studies have also documented underuse of calcium and vitamin D supplementation. A review found that approximately 30 % of

patients at a large health maintenance organization in the U.S. on glucocorticoids received calcium and vitamin D.[8] In 2002, Solomon et al.[9] examined management practices for patients with rheumatoid arthritis taking glucocorticoids at one academic medical rheumatology practice and found that only 25 % of patients had calcium and/or vitamin D recorded on the medication list. Curtis et al.[10] reviewed a database of patients on glucocorticoids from a national managed care organization and reported that 51 % of physicians, across all specialties, prescribed calcium and vitamin D, and 55 % of rheumatologists prescribed calcium and vitamin D. A retrospective chart review of 100 patients receiving long-term glucocorticoids at an academic Veterans Affairs (VA) Medical Center revealed that 32 patients were prescribed calcium supplementation and 12 patients were prescribed vitamin D.[11]

Several interventions have been developed to improve adherence to recommendations to prevent GIOP.[12–14] At one US academic center, a trial randomized 21 rheumatologists caring for 373 chronic glucocorticoid users to an intervention consisting of a lecture, discussion and confidential physician audit of practice patterns.[12] No subsequent differences in the rates of prescribed therapies for GIOP were observed in the intervention group compared with the control group.

Using administrative databases of a large US health plan, another prospective study randomized 153 physicians (following 799 patients on chronic glucocorticoids) to receive a web-based GIOP education module, feedback on rates of past GIOP testing and treatment, and a GIOP-specific quality improvement management algorithm, or to a control intervention, which included three modules of text-based traditional continuing medical education modules focused on non-adherence to practice guidelines in chronic disease and clinical prediction rules. The intervention did not improve adherence to guidelines to prevent or treat GIOP.[13]

Naunton et al.[14] attempted to improve the quality of care for patients who were at risk for GIOP using an intervention consisting of educational materials and management guidelines sent to all general practitioners and community pharmacies within a defined geographic region. The intervention also included patient and provider reminders and academic detailing visits whereby local experts directly reviewed guidelines with both practitioners and pharmacists. Although a modest improvement in the use of osteoporosis preventive therapies was observed [calcium (5 % to 19 %), vitamin D (3 % to 11 %) and bisphosphonates (6 % to 24 %)] following this multifaceted intervention, this study was limited to patients presenting for hospital admission.

With the passage of the U.S. Health Information Technology for Economic and Clinical Health Act, the use of medication management information technology to improve medication management, patient safety and the "meaningful use" of electronic health records has increased the number of facilities that are using clinical decision support and computerized provider order entry systems for e-prescribing, drug-drug and drug-allergy checking, and medication reconciliation.[15] A recent systematic review of randomized controlled trials studying the effectiveness of clinical decision support and computerized provider order entry systems showed that changes utilizing information technology are more likely to affect provider behavior and improve the delivery of care than traditional continuing education programs.[16]

The objective of this study was to determine whether an automated prescription order set that co-prescribes calcium and vitamin D with glucocorticoids (and enables providers to opt out of the system by modifying the order) increases the number of co-prescriptions for calcium and vitamin D for patients on glucocorticoids. We chose to use an automated order set as opposed to a clinical reminder, because the former is easier for clinicians to use and the latter would need to compete with multiple other reminders.

METHODS

Intervention

The study was performed at a single VA medical center. The VA uses a national computerized provider order entry system called Computerized Patient Record System (CPRS). All orders for patients, including medication prescriptions, are entered into CPRS through one of three mechanisms (order dialogs, quick orders and order sets).[17] For this study, the CPRS order set for glucocorticoids, specifically prednisone, was modified by the pharmacy to create a "guided medication ordering pathway." Prednisone was removed from the general selection medication ordering list and identified for ordering only through a defined pathway. Pathways were set up for both inpatient and outpatient orders so that providers would not have to use two different order sets for glucocorticoid prescriptions. However, only outpatients were included in this study.

The automated prescription order set was for 1,500 mg of oral calcium carbonate and 1,000 international units (IU) of vitamin D (cholecalciferol) daily. This order appeared each time a provider ordered oral glucocorticoids. This combination of calcium and vitamin D was chosen because it is the most economical in the VA formulary. The doses of calcium and vitamin D were chosen based on the American College of Rheumatology 2010 recommendations for the prevention and treatment of GIOP.[1] The default order was a single prescription for 90 days (to minimize co-pays). Providers were allowed to edit or cancel orders by unchecking the appropriate boxes. An option for community pharmacy orders of calcium and vitamin D was included to accommodate patients who use non-VA pharmacies.

Before the automated order set was generated, providers were required to answer an electronic query about whether their patients were known to have hypercalcemia. The default option for calcium and vitamin D supplementation was not generated for patients identified by providers as having known hypercalcemia. Providers were made aware of the intended automated CPRS changes for calcium and vitamin D through repeated emails prior to the launch of the new automated order set.

Data Collection

We performed a pre-post test study by examining the proportion of subjects on glucocorticoids receiving calcium and vitamin D supplementation during the 12-month period before (T1) and after (T2) the order set was implemented. T2 began after a 3-month lag period, during which providers were sent a series of emails to alert them to the upcoming change in order sets. A separate database search was performed for all patients who had one or more orders of glucocorticoids of at least 2-week duration during T1 and T2. The 2-week cutoff was chosen in consultation with the primary care providers at our institution in order to prevent the order set from appearing for patients receiving a single glucocorticoid prescription for an acute illness such as an allergic reaction. The earliest glucocorticoid order was chosen for those patients with multiple prescriptions. A chart review was performed to ascertain patient demographic characteristics (age, race, gender), body mass index, comorbidities as measured by the Charlson comorbidity index (CCI),[18] reported diagnosis of osteoporosis, history of osteoporotic fracture, tobacco and alcohol use, orders for glucocorticoids (prednisone), duration of time (days) on glucocorticoids, orders for calcium and vitamin D, duration of time on calcium and vitamin D, specialty of the provider, level of the provider (attending, fellow, resident, physician assistant/nurse practitioner) ordering glucocorticoids and presence of hypercalcemia. Multivitamins were not considered as calcium or vitamin D supplementation. Over-the-counter medications are routinely recorded using a specific template within the VA electronic medical record.

Statistical Analyses

We performed descriptive analyses of all collected variables. Differences in variables between pre- and post- intervention periods were evaluated using chi-square or t-tests as appropriate. Multivariate logistic regression was then used to examine the effects of the intervention adjusting for the period(s) during which co-prescriptions were received as well as the variables that differed (at $p<0.05$) between T1 and T2. Levels of prescriber were treated as dummy variables with attendings serving as the referent category. After seeing the modest impact of the intervention, brief follow-up queries were conducted among consecutive providers identified as frequent non-prescribers of calcium and vitamin D to determine possible reasons for non-adherence to GIOP guidelines. The protocol was approved by the Human Subjects Committee at our institution.

RESULTS

Five hundred thirty-five outpatients had a glucocorticoid prescription of at least 2-week duration during T1 and 506 outpatients had a glucocorticoid prescription of at least 2-week duration during T2. Of these patients, 258 had a glucocorticoid prescription in T1 only, 221 had a glucocorticoid prescription in T2 only, and 562 had glucocorticoid prescriptions in both T1 and T2. One patient with hypercalcemia was identified during T1, and two were identified in T2. The most frequent prescribers of glucocorticoids were providers in internal medicine/primary care 480 (46 %) and in the rheumatology 179 (17 %) and pulmonary 63 (6 %) subspecialties. Patient demographic and clinical characteristics did not differ across time periods (Table 1). However, the level of the provider prescribing glucocorticoids did differ between T1 and T2.

The percent of co-prescriptions for calcium increased from 37 % to 49 % ($p<0.0001$) and vitamin D increased from 38 % to 53 % ($p<0.0001$) after the new order set was implemented. The difference in co-prescriptions across time periods remained significant after controlling for the level of provider prescribing glucocorticoids, having a rheumatologist prescribing glucocorticoids, and for the period(s) during which co-prescriptions were received [adjusted odds ratio (95 % CI)=1.74 (1.34-2.24) and 1.89 (1.47-2.45) for calcium and vitamin D, respectively].

We interviewed ten providers (two rheumatology fellows, four primary care attending physicians, two internal medicine residents, one orthopedic surgery resident, one general medicine mid-level provider) at the end of the study. The only reason offered by providers for deleting co-prescriptions for calcium and vitamin D was a lack of awareness of any "strong" evidence supporting recommendations to co-prescribe calcium and vitamin D when glucocorticoids are prescribed for less than 3 months.

DISCUSSION

In this study, implementation of an automated order set significantly increased the number of co-prescriptions for calcium and vitamin D in patients who are prescribed glucocorticoids for at least 2 weeks. The results are encouraging given the numerous interventions that have failed to improve adherence to GIOP guidelines.

While we found a statistically significant difference, the impact of the intervention was relatively modest. Despite

Table 1. Patient Characteristics During T1 and T2

Variables	T1 (total=535) N (%)	T2 (total=506) N (%)	p-value
Age, years (mean ± SD)	68.3±13.6	68.5±13.8	0.8
Male	508 (95.0)	484 (95.7)	0.6
White	470 (87.9)	439 (86.8)	0.6
BMI≥30	220 (41.1)	223 (44.1)	0.3
Charlson comorbidity score≥2	346 (64.7)	330 (65.2)	0.9
Glucocorticoid dose, mg/day (mean ± SD)	5.1±8.0	5.5±7.0	0.4
Glucocorticoid duration, days (mean ± SD)	192 (233.0)	210 (174.0)	0.1
Diagnosis of osteoporosis	49 (56.6)	46 (9.1)	1.0
Current tobacco use	60 (11.2)	48 (9.5)	0.4
Current alcohol use	23 (4.3)	13 (2.6)	0.1
History of osteoporotic fracture	17 (3.2)	20 (4.0)	0.5
Current use of bisphosphonate	78 (14.6)	72 (14.2)	0.9
Hypercalcemia	1 (0.2)	2 (0.4)	0.5
Bone densitometry performed	147 (14.1)	136 (26.9)	0.8
Glucocorticoids prescribed by a rheumatologist	82 (15.3)	97 (19.2)	0.1
Level of provider prescribing glucocorticoids			0.03
Resident	84 (15.7)	51 (10.1)	
Fellow	107 (20.0)	95 (18.8)	
Attending	309 (57.8)	330 (65.2)	
Physician assistant or nurse practitioner	35 (6.5)	30 (5.9)	
Calcium and vitamin D prescribed by a rheumatologist*	16 (21.3)	36 (22.1)	0.9
Level of provider prescribing calcium and vitamin D*			0.4
Resident	14 (18.7)	26 (15.9)	
Fellow	23 (30.7)	46 (28.2)	
Attending	33 (44.0)	86 (52.8)	
Physician assistant or nurse practitioner	5 (6.7)	5 (3.1)	

**Of a total of 75 patients prescribed calcium and vitamin D during T1 and 238 in T2*

the intervention, many patients remain undertreated, with approximately half of the eligible patients receiving supplementation. Though we did not perform a formative evaluation of the intervention, interviews with several of the providers at our institution revealed that a major barrier toward co-prescription was rejection of the recommendation to co-prescribe calcium and vitamin D in patients expected to receive less than 3 months of glucocorticoids because of lack of direct evidence supporting this approach. Guidelines frequently differ between organizations, and it is possible (although not proven) that thresholds for instituting preventative measures may vary by specialty. While we did not record consecutive days, the mean number of days on glucocorticoids was approximately 200. Thus, it is likely that many patients remain undertreated, even at the 3-month threshold, perhaps because of unanticipated prescription renewals.

The feedback received from the providers highlights the importance of stakeholder involvement and transparency in the creation and dissemination of guidelines. The GRADE approach (http://www.gradeworkinggroup.org/) classifies recommendations as "strong" or "weak" based on whether clinicians judge the benefits to clearly outweigh the risk and burdens related to treatment and thereby consider other factors in addition to the strength of evidence when rating the strength of specific recommendations. This approach allows for a "strong" recommendation despite the lack of randomized controlled trial evidence. For example, avoiding the use of aspirin in children with febrile illnesses to decrease the risk of Reye's syndrome would be classified as a strong recommendation despite the lack of direct evidence supporting this statement. Future versions of GIOP guidelines would be strengthened by adopting this approach.

We chose to use an automated prescription order set for calcium and vitamin D supplementation because this approach enables physicians to take advantage of a preprogrammed default option. Clinical decision support systems (CDSS) have been increasingly used to improve clinical provider performance in adherence to recommended guidelines.[19,20] Kawamoto et al.[21] reviewed the ability of CDSS to improve clinical practice and identified important features that improved the success rate of CDSS interventions. Seventy-five percent of interventions succeeded when the decision support was provided to clinicians automatically, whereas none succeeded when clinicians were required to seek out advice of the decision support system. Systems that were provided as an integrated component of charting or order entry systems were significantly more likely to succeed than stand-alone systems (rate difference 37 %). And systems that used a computer to generate the decision support were significantly more effective than those relying on manual processes (rate difference 26 %). Our intervention was designed according to these principles, and it led to improvement in prescribing calcium and vitamin D for glucocorticoid users.

Limitations of this study include the design of this study: this was a pre-post intervention, not a randomized controlled trial. However, it is unlikely that the change in supplement-ordering behavior was due to anything other than our intervention, as apart from the emails notifying providers of the new order set, there were no other educational campaigns, institutional changes or major publications promoting this behavior change during the study time period. Generalizability is limited as the intervention was tested in a single site and the majority of patients were men. Moreover, the study was conducted in a health-care setting in which

providers are accustomed to computerized decision support tools. Future implementation trials are required to test the value of this approach in settings other than the VA.

Missing data, most notably related to over-the-counter use of supplements, are always a concern. However, the VA explicitly records the use of all medications, including over-the-counter medications and supplements obtained outside of the VA. It is also unlikely that missing data would differ systematically across both time periods. To the best of our knowledge, there were no unintended consequences related to changing the order sets. Lastly, while process measures are important, ultimately, the most clinically desirable outcome to assess from this intervention would be bone densitometry and GIOP-related fractures.

CONCLUSIONS

Implementation of an automatic prescription order set significantly improves co-prescription of calcium and vitamin D in patients who are prescribed glucocorticoids. Hypercalcemia is not a limiting factor in co-prescription. However, advanced programming to block the order set in patients with high calcium levels would eliminate the need for physicians to check for hypercalcemia. The lack of evidence-based data supporting calcium and vitamin D supplements for any duration of glucocorticoid use is a significant barrier to adherence to GIOP guidelines advocating the use of calcium and vitamin D supplementation for all patients prescribed glucocorticoids regardless of the intended duration. Given the limitations related to the study design and generalizability, these results should not be interpreted as prescriptive, but should serve to inform the design of future implementation trials.

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REFERENCES

1. **Grossman JM, Gordon R, Ranganath VK, et al.** American College of Rheumatology 2010 Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res. 2010;62:1515–26.
2. **Lane NE, Lukert B.** The science and therapy of glucocorticoid-induced bone loss. Endocrinol Metab Clin North Am. 1998;27:465–83.
3. **Van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C.** Oral corticosteroids and fracture risk: relationship to daily and cumulative doses. Rheumatology (Oxford). 2000;39:1383–9.
4. **Van Staa TP, Geusens P, Pols HA, de Laet C, Leufkens HG, Cooper C.** A simple score for estimating the long-term risk of fracture in patients using oral glucocorticoids. QJM. 2005;98:191–8.
5. **Adachi JD, Benson WG, Bianchi F, et al.** Calcium and vitamin D supplementation prevents bone loss in the spine secondary to low dose corticosteroids. J Rheumatol. 1996;125:995–1000.
6. **Buckley LM, Leib ES, Cartularo KS, et al.** Calcium and vitamin D3 supplementation prevents bone loss in the spine secondary to low-dose corticosteroids in patients with rheumatoid arthritis. Ann Intern Med. 1996;125:961–8.
7. **Dyksman TR, Haralson KM, Gluck OS, et al.** Effect of oral 1, 25-dihydroxyvitamin D and calcium on glucocorticoid-induced osteopenia in patients with rheumatic diseases. Arthritis Rheum. 1984;27:1336–43.
8. **Yood RA, Harrold LR, Fish L, et al.** Prevention of glucocorticoid-induced osteoporosis: experience in a managed care setting. Arch Intern Med. 2001;161:1322–7.
9. **Solomon DH, Katz JN, Jacobs JP, La Tourette AM, Coblyn J.** Management of glucocorticoid-induced osteoporosis in patients with rheumatoid arthritis: rate and predictors of care in an academic rheumatology practice. Arthritis Rheum. 2002;46:3136–42.
10. **Curtis JR, Westfall AO, Allison J, et al.** Challenges in improving the quality of osteoporosis care for long-term glucocorticoid users. Arch Intern Med. 2007;167:591–6.
11. **Guzman-Clark JR, Fang MA, Sehl ME, Traylor L, Hahn TJ.** Barriers in the management of glucocorticoid-induced osteoporosis. Arthritis Rheum. 2007;57:140–6.
12. **Solomon DH, Katz JN, La Tourette AM, Coblyn JS.** Multifaceted intervention to improve rheumatologists' management of glucocorticoid-induced osteoporosis. J Rheumatol. 2004;51:383–7.
13. **Curtis JR, Westfall AO, Allison JJ, et al.** Longitudinal patterns in the prevention of osteoporosis in glucocorticoid-treated patients. Arthritis Rheum. 2005;52:2485–94.
14. **Naunton M, Peterson GM, Jones G, Griffin GM, Bleasel MD.** Multifaceted educational program increases prescribing of preventive medication for corticosteroid induced osteoporosis. J Rheumatol. 2004;31:550–6.
15. **Blumenthal D, Tavenner M.** The "meaningful use" regulation for electronic health records. N Engl J Med. 2010;363:501–4.
16. **McKibbon KA, Lokker C, Handler SM, et al.** The effectiveness of integrated health information technologies across the phases of medication management: a systematic review of randomized controlled trials. JAMIA. 2012;19:22–30.
17. **Payne TH, Hoey PJ, Nichol P, Lovis C.** Preparation and use of preconstructed orders, order sets, and order menus in a computerized provider order entry system. J Am Med Inform Assoc. 2003;10:322–9.
18. **Charlson ME, Pompei P, Ales KL, MacKenzie CR.** A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis. 1987;40:373–83.
19. **Haynes RB, Wilczynski NL, Computerized Clinical Decision Support System (CCDSS) Systematic Review Team.** Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: methods of a decision-maker-researcher partnership systematic review. Implement Sci. 2010;5:12.
20. **CCDSS Systematic Review Team, Hemens BJ, Holbrook A, Tonkin M, Mackay JA, Weise-Kelly L, Navarro T, Wilczynski NL, Haynes RB.** Computerized clinical decision support systems for drug prescribing and management: A decision-maker-research partnership systematic review. Implement Sci. 2011;6:89.
21. **Kawamoto K, Houlihan CA, Balas EA, Lobach DF.** Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ. 2005;330:765.