Prevention of Glucocorticoid-Induced Osteoporosis

Experience in a Managed Care Setting

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Background: Treatment with glucocorticoids is the leading cause of drug-induced osteoporosis. Currently available guidelines indicate that patients receiving long-term glucocorticoid therapy should receive measures to prevent osteoporosis.

Objectives: To examine whether patients receiving long-term glucocorticoid therapy in a managed care setting received preventive therapy or prescribed medications for osteoporosis and to identify patient and provider characteristics associated with treatment.

Subjects and Methods: A cohort of 224 health plan enrollees 20 years and older who were dispensed at least 1 oral glucocorticoid prescription per quarter during the period October 1997 through September 1998 was identified from administrative data. Medical charts and administrative data were reviewed to determine use of preventive therapy and prescribed medications for osteoporosis.

Results: Of the 224 patients, 62% had at least 1 documented intervention aimed at osteoporosis prevention (counseling about calcium or vitamin D or weight-bearing exercise; prescription for estrogen, calcitonin, or bisphosphonate; or a bone mineral density study). Women were more likely than men to receive intervention (76% vs 44%; prevalence odds ratio, 4.41; 95% confidence interval, 2.17-9.10). Patients receiving a mean daily prednisone dose of 10 mg or more or 5 to less than 10 mg were no more likely to receive intervention than those receiving 5 mg or less prednisone daily. Sixty-two (90%) of 69 patients who were prescribed glucocorticoid therapy by rheumatologists had at least 1 intervention documented compared with 29 (48%) of 60 for internists, 26 (55%) of 47 for pulmonologists, and 22 (46%) of 48 for all other physicians. In a multiple logistic regression model, including patient age, sex, mean daily glucocorticoid dose, and physician specialty, women and patients prescribed glucocorticoids by a rheumatologist were significantly more likely to receive intervention aimed at osteoporosis prevention.

Conclusions: A substantial proportion of patients receiving long-term glucocorticoid therapy do not receive preventive therapy for osteoporosis. Efforts should be made to reduce barriers to such treatment and increase the proportion of patients given preventive therapy.

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Although glucocorticoid therapy is used extensively to treat a variety of diseases, in recent years, it has become apparent that even low-dose glucocorticoid therapy may result in bone loss. In addition to causing bone loss, glucocorticoids appear to lead to changes in the architectural integrity of bone. Consequently, more than one fourth of patients treated with long-term glucocorticoid therapy sustain osteoporotic fractures. Many treatments have been shown to prevent glucocorticoid-induced osteoporosis. Calcium and vitamin D (cholecalciferol) should be used by all patients receiving long-term glucocorticoid therapy and may be sufficient for some, especially those receiving lower-dose glucocorticoid therapy (≤7.5 mg of prednisone daily) or those who have normal bone density at the start of therapy. Hormonal replacement therapy prevents bone loss and may increase bone density in patients treated with glucocorticoids. In men, testosterone replacement for patients with low testosterone levels results in increased bone density. Calcitonin may also be helpful in prophylaxis of glucocorticoid-induced osteoporosis, although some studies show at most a modest benefit over calcium and vitamin D alone. The strongest data available involve the use of bisphosphonates, including etidronate, alendronate, and risedronate, which have been shown to maintain or increase bone density and in some
SUBJECTS AND METHODS

STUDY SETTING

The Fallon Community Health Plan is a mixed-model health maintenance organization operating in central and eastern Massachusetts since 1977. The group-model component of the health maintenance organization (that portion of the health maintenance organization that contracts with a medical group for the health care services for members) is composed of a large multispecialty group practice with more than 200 physicians providing care to approximately 150000 members. More than 90% of the health plan members are covered by a drug benefit plan, with a nominal copayment for each prescription. For members who make out-of-pocket purchases of drugs, prescriptions are favorably priced at or near the average wholesale price for the agent. Over-the-counter medications are not covered for any members.

The computerized information system of the health plan contains records on utilization of all health care services and prescriptions filled, which are collected as part of routine fiscal activities, as well as the results of laboratory and radiological studies. Each prescription record contains a unique patient identification number as well as the medication name, the date the prescription was filled, the number of tablets dispensed, and the dose per tablet. Although the use of the automated database allowed us to confirm that a patient actually filled a prescription, we were not able to determine if there were instances in which prescriptions were written but not filled by the patient. Information relating to over-the-counter medications is not available through the computerized information system.

STUDY POPULATION AND CHARACTERISTICS

The study population was composed of all members of the health plan in the group-model component. Members included those 20 years and older who were continuously enrolled between October 1, 1997, and September 30, 1998; were dispensed at least 1 prescription for an oral glucocorticoid per quarter; and had confirmation of glucocorticoid use in the medical record. Automated databases were used to ascertain information about glucocorticoid prescriptions as well as prescriptions for prophylactic medications. Patients who received at least 1 dispensing of an oral estrogen, etidronate, alendronate, testosterone, or intranasal or subcutaneous calcitonin between October 1, 1997, and September 30, 1998, were characterized as having medical treatment for prevention of glucocorticoid-induced osteoporosis. Medical record review was performed by trained nurse reviewers, who collected information on the diagnosis requiring glucocorticoid treatment, prescribing physician specialty, documentation of patient education concerning calcium and vitamin D supplementation as well as weight-bearing exercise, and performance of bone mineral density testing (if done).

The mean prednisone equivalent dose was calculated based on the total amount of the drug dispensed by the pharmacy from the date of the first prescription until the last dispensing in the 1-year study period. For patients who were prescribed methylprednisolone, the prednisone equivalent dose was calculated at 1.25 mg of prednisone per 1 mg of methylprednisolone.

STATISTICAL ANALYSIS

χ² Tests were used to evaluate differences in proportions. All tests of significance were 2-tailed and P < .05 was considered significant. To identify factors independently associated with the use or recommendation of any preventive intervention, we constructed a multiple logistic regression model. Factors included in the model were the following: patient age (<75 years vs ≥75 years); sex (women vs men); mean daily glucocorticoid dose (≥5 mg/d vs <5 mg/d); and physician specialty (rheumatology vs other).

RESULTS

There were 152818 members of the health plan continuously enrolled in the group-model component from October 1, 1997, through September 30, 1998. Of these, 113401 were 20 years or older. There were 228 patients dispensed at least 1 oral glucocorticoid prescription per quarter during this period. Four of these were excluded from the study population (2 had no documentation of glucocorticoid use in the medical record and the medical records of 2 patients could not be retrieved). The mean ± SD age of the patients was 70 ± 15 years (Table 1): 29% were younger than 65 years; 23% were 65 to 74 years; and 48% were 75 years or older. Fifty-seven percent of the patients were women. The most common diagnoses associated with
the use of glucocorticoid therapy were chronic obstructive pulmonary disease (26%), asthma (23%), rheumatoid arthritis (22%), and polymyalgia rheumatica (12%) (Table 1). Some patients had more than 1 condition that required glucocorticoid treatment. The specialty of the treating physician is described in Table 1. The mean ± SD daily glucocorticoid dose among the study subjects was 8.9 ± 7.3 mg of prednisone or equivalent. Seventy patients (31%) received a mean daily prednisone dose less than 5 mg, 88 (39%) took 5 to less than 10 mg of prednisone, and 66 (29%) took 10 mg or more of prednisone daily during the study.

The frequencies of medical record documentation of counseling on the need for calcium and vitamin D supplementation and weight-bearing exercise are summarized in Table 2. Women were more likely than men to have received education on the need for calcium and vitamin D (prevalence odds ratio [OR], 3.58; 95% confidence interval [CI], 1.91-6.75 and OR, 4.05; 95% CI, 2.11-7.83, respectively). The use of bone mineral testing and pharmacological intervention are also described in Table 2. No patient was prescribed testosterone during the study period. Women were more likely than men to have bone mineral density tests (43% vs 15%; prevalence OR, 4.41; 95% CI, 2.17-9.10). Women were also more likely than men to have at least 1 intervention (76% vs 44%; prevalence OR, 4.02; 95% CI, 2.19-7.43). When patients were categorized according to 3 levels of mean daily prednisone dose (<5 mg, 5 to <10 mg, or ≥10 mg), those taking higher doses of prednisone were found to be less likely to have received education on vitamin D and exercise (test for trend, P = .05). However, there were no differences for education on calcium, bone mineral density testing, or drug therapy based on glucocorticoid dose (Figure).

Sixty-two (90%) of 69 patients who received glucocorticoid prescriptions from rheumatologists had at least 1 intervention documented compared with 29 (48%) of 60 for internists, 26 (53%) of 47 for pulmonologists, and 22 (46%) of 48 for all other specialties (Table 3). Fifty-five patients (25%) were given prescription medications for osteoporosis. Of these, 25 were prescribed hormone replacement therapy, 14 calcitonin, 6 etidronate, and 17 alendronate, with some patients having received more than 1 drug during the study period.

The findings of the multiple logistic regression model that simultaneously included patient age, sex, mean daily glucocorticoid dose, and physician specialty suggested that patient sex and physician specialty were independently associated with the use or recommendation of a preventive therapy. Women receiving long-term glucocorticoid therapy were significantly more likely to use or receive a recommendation for a preventive therapy (OR, 3.05; 95% CI, 1.65-5.66). Patients who were prescribed glucocorticoids by rheumatologists were significantly more likely to use or receive a recommendation for a preventive therapy compared with those who were prescribed these agents by physicians in other specialties (OR, 6.70; 95% CI, 2.78-16.19). After inclusion in the multiple logistic regression model, patient age and glucocorticoid dose were not found to be significantly associated with the use of preventive therapy.

### Table 1. Demographic Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Age, mean ± SD, y</th>
<th>70 ± 15</th>
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</thead>
<tbody>
<tr>
<td>Women, No. (%)</td>
<td>128 (57)</td>
</tr>
<tr>
<td>Diagnosis, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>59 (26)</td>
</tr>
<tr>
<td>Asthma</td>
<td>51 (23)</td>
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<tr>
<td>Rheumatoid arthritis</td>
<td>49 (22)</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>26 (12)</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Renal transplant</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Wegener granulomatosis</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Crohn disease</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Other</td>
<td>42 (19)</td>
</tr>
<tr>
<td>Prednisone dose, mean ± SD, mg</td>
<td>8.9 ± 7.3</td>
</tr>
<tr>
<td>Specialty of prescribing physician, No. (%)</td>
<td></td>
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<tr>
<td>Rheumatology</td>
<td>69 (31)</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>60 (27)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>47 (21)</td>
</tr>
<tr>
<td>Other</td>
<td>48 (21)</td>
</tr>
</tbody>
</table>

*Because patients may have had more than 1 condition associated with treatment with glucocorticoids, the numbers and percentages do not add to 224 and 100%, respectively.
†Includes all conditions with 3 or fewer patients with the following diagnoses: ulcerative colitis, undifferentiated inflammatory bowel disease, polyarteritis nodosa, hemolytic anemia, myasthenia gravis, multiple sclerosis, sarcoidosis, Sjogren syndrome, psoriatic arthritis, polymyositis, polychondritis, lymphoma, immune thrombocytopenic purpura, interstitial lung disease, gout, tenosynovitis, allergic reaction, leukemia, and dermatologic conditions.

### Table 2. Patient Education, Screening, and Treatment for Osteoporosis of Study Subjects

<table>
<thead>
<tr>
<th>Calcium†</th>
<th>Vitamin D‡</th>
<th>Exercise§</th>
<th>Bone Mineral Density¶</th>
<th>Drug Therapy¶</th>
<th>Any Intervention§ #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (n = 128)</td>
<td>66 (52)</td>
<td>64 (50)</td>
<td>20 (16)</td>
<td>55 (43)</td>
<td>45 (35)</td>
</tr>
<tr>
<td>Men (n = 96)</td>
<td>22 (23)</td>
<td>19 (20)</td>
<td>14 (15)</td>
<td>14 (15)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Total (N = 224)</td>
<td>88 (39)</td>
<td>83 (37)</td>
<td>34 (15)</td>
<td>69 (31)</td>
<td>55 (25)</td>
</tr>
</tbody>
</table>

*All values are number (percentage).
†Includes education on adequate calcium intake either via dietary sources or supplements.
‡Includes education on adequate vitamin D intake.
§Includes recommendations for weight-bearing exercise.
¶Includes documentation of a bone mineral density study.
#Includes any person who had at least 1 of the interventions (this includes calcium or vitamin D education, exercise recommendations, performance of a bone mineral density study, or drug therapy).
While 62% of patients receiving long-term glucocorticoid therapy during the course of the study year had at least 1 documented intervention aimed at osteoporosis prevention (counseling on calcium or vitamin D or weight-bearing exercise; prescription for estrogen, calcitonin, or bisphosphonate; or bone mineral density study), only 31% had a bone mineral density study, and only 40% had documentation of calcium supplementation and 37% vitamin D supplementation. Our results for calcium and vitamin D supplementation are similar to the results of Aagaard et al, who found that 42% of patients received calcium and 37% vitamin D. Of the eligible postmenopausal women in that study, 57% received hormone replacement therapy, although it could not be determined if the hormone replacement therapy was prescribed solely for osteoporosis prophylaxis or for other reasons. Only 20% of the treatment regimens in the study by Aagaard and coworkers were for bisphosphonate therapy compared with 37% in our study. Given that bisphosphonates appear to be more effective drugs for prevention of glucocorticoid-induced osteoporosis, the higher use of bisphosphonates in our population may be the more appropriate therapeutic approach to this clinical situation. This higher use of bisphosphonates may relate to the high levels of insurance coverage for pharmaceuticals among our population and the increasing awareness of the benefits of this therapy.

Guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis have been published by an American College of Rheumatology Task Force on Osteoporosis Guidelines as well as by a United Kingdom consensus group. Clearly a large number of patients are not receiving intervention for prevention or treatment according to those guidelines. The reasons for this may include patient-, physician-, and health care system–related barriers. As suggested in our study and others, patient-related factors include sex and postmenopausal state. Our study confirms previous reports that women are more likely than men to receive preventive therapy. Other factors may include the underlying disease for which the glucocorticoid is prescribed, the severity of illness, comorbidities, and willingness of the patient to take medication perceived as having a high frequency of adverse effects (hormone replacement therapy) or as being inconvenient and expensive (bisphosphonates).

Physician-related barriers likely include a lack of recognition of the frequency of glucocorticoid-induced osteoporotic fractures or a lack of awareness of the existence and effectiveness of prophylactic therapy. Physicians may be uncertain about which patients require treatment. For example, the American College of Rheumatology guidelines suggest pharmacological intervention (in addition to calcium and vitamin D) for patients whose bone density T score is −1 or lower, while the United Kingdom Consensus Task Force guidelines recommend treatment for those with a T score less than −1.5. Physicians may believe that there is a safe dose of glucocorticoid, so there may not be a consensus that patients taking lower doses of prednisone (eg, ≤7.5 mg) are at risk for osteoporosis. However, in our study, patients in the higher-dose glucocorticoid therapy groups were no more likely to receive osteoporosis prophylaxis than patients in the lower-dose group.

Patients who receive care from rheumatologists are more likely to receive prophylactic care, suggesting that rheumatologists may be more aware of risks and treatment options than other physicians. Specialists may have greater access to newer information than generalists. As is the case of the American College of Rheumatology guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis, such guidelines are often published in journals that target specialists. As most of the studies of treatment for osteoporosis are of women, physicians may not be convinced that prophylaxis for men is necessary. Some studies have suggested that physicians tend to underprescribe beneficial prophylactic therapy for the elderly population. In addition, physicians focused on treatment of an underlying

### Table 3. Patient Education, Screening, and Treatment for Osteoporosis of Study Subjects by Specialty of the Prescribing Physician

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Calcium</th>
<th>Vitamin D</th>
<th>Exercise</th>
<th>Bone Mineral Density</th>
<th>Drug Therapy</th>
<th>Any Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatology (n = 69)</td>
<td>44 (64)</td>
<td>44 (64)</td>
<td>16 (23)</td>
<td>39 (57)</td>
<td>27 (39)</td>
<td>62 (90)</td>
</tr>
<tr>
<td>Internal medicine (n = 60)</td>
<td>16 (27)</td>
<td>11 (18)</td>
<td>8 (13)</td>
<td>6 (10)</td>
<td>11 (18)</td>
<td>29 (48)</td>
</tr>
<tr>
<td>Pulmonary (n = 47)</td>
<td>17 (36)</td>
<td>16 (34)</td>
<td>5 (11)</td>
<td>13 (35)</td>
<td>11 (23)</td>
<td>26 (55)</td>
</tr>
<tr>
<td>All others (n = 48)</td>
<td>11 (23)</td>
<td>12 (25)</td>
<td>5 (10)</td>
<td>15 (31)</td>
<td>6 (13)</td>
<td>22 (46)</td>
</tr>
</tbody>
</table>

*All values are number (percentage). See second to seventh footnotes to Table 2 for description of preventive measures.*
serious disease may be less likely to address preventive health care issues. Physicians may also be concerned that additional medications may increase the risk of adverse drug events and decrease patient compliance with essential therapy.

Health care system–related barriers may include the cost and availability (or lack thereof) of bone mineral density testing and the cost of prophylactic medication, which may be substantial. In our managed care population, that cost was assumed by the insurer, but in other settings, the cost of prophylaxis may be the responsibility of the patient or another third party. In addition, many patients who require glucocorticoid therapy are under the care of 1 or more specialists with or without a primary care physician, and this fragmentation of care may result in less use of prophylactic therapy.

Several strengths and limitations of our study deserve mention. This study was performed using a managed care database that allowed us to identify all patients who received prescription medication at the organization’s pharmacies. We did not rely on recorded lists of medication use in the medical record, which may be discrepant with the medications patients actually take. Similarly, while we could not identify patients who filled their prescriptions at outside pharmacies, we believe that the cost to the patient of using an outside noncovered pharmacy is such that the pharmacy records are virtually complete. We did rely on the medical record to determine use of nonprescription calcium and vitamin D. Physicians may not reliably document use of nonprescription medications, so our results may be an underestimate of the use of calcium and vitamin D.

Another potential limitation concerns the calculation of the glucocorticoid dose. We calculated the mean daily dose based on the total dose prescribed during the time from the first to the last prescription in the study period. Because some patients may have taken their medication intermittently, we may have underestimated the daily (but not total) dose. We also could not determine from our study if hormone replacement therapy was prescribed for prevention of osteoporosis or for other reasons.

In conclusion, while effective regimens for the prevention and treatment of glucocorticoid-induced osteoporosis exist, many patients do not receive such treatment. The reasons for this are probably complex, including patient-, physician-, and health care system–related barriers. Health care organizations should consider the use of various mechanisms to educate and alert physicians as to the need for preventive therapy for patients receiving long-term glucocorticoid therapy. Educational efforts may include the recruitment of local medical opinion leaders into systematic quality improvement initiatives. Efforts to alert physicians to the need for intervention may include the use of physician prompts to notify the physician that intervention may be needed for a particular patient. Through efforts aimed at reducing barriers to treatment, the quality of care for patients receiving long-term glucocorticoid therapy may be improved.

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REFERENCES


