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Evaluation of an Outpatient Pharmacy Clinical Services Program on Adherence and Fractures among Patients with Osteoporosis

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Purpose

Prior research has shown that low adherence to osteoporosis medications is associated with increased fracture risks. The objective of this study was to evaluate the impact of an outpatient pharmacy clinical service (OPCS) on medication adherence and fractures among patients with osteoporosis.

Methods

This study compared patients who received OPCS consultations upon picking up a new osteoporosis prescription at Kaiser Permanente Orange County pharmacies to usual care patients without an OPCS consultation. Three patients from the usual care group were matched to each patient in the OPCS program based on age, gender and whether or not they had a previous medication for osteoporosis within six months before the index date (new or prior users). Medication adherence and risk of fracture were compared using multivariate logistic regression. The analysis was conducted for the full cohort and by new and prior users.

Results

Among 1,172 OPCS and 3,302 usual care patients, we found no significant difference in adherence between OPCS and usual care patients in the full cohort or among prior users. Among new users, the OPCS group was significantly more likely to be medication adherent compared to the usual care group (OR = 1.23; 95% CI 1.05 – 1.44; p =0.012). We found no significant differences in risk of fracture.

Conclusion

Outpatient pharmacists are in a strategically excellent position to implement case management strategies to improve suboptimal adherence for patients with osteoporosis. Patients who initiate medications may be the best candidates for such interventions.

Introduction

Despite the favorable efficacy associated with osteoporosis medications, patient adherence remains suboptimal. Adherence rates to osteoporosis medications range from about 40 to 70 percent.[1] Reasons for nonadherence are numerous and may include medication side effects, dosing requirements, and a perceived lack of benefit for an asymptomatic disease. Poor adherence is associated with increased fracture risks, and interventions designed to reduce fractures, including improved medication adherence, can ultimately improve quality of life and help curb osteoporosis-related costs.[2,3]

Because of their specialized knowledge of medications and access to patients, outpatient pharmacists are well positioned to coach patients in overcoming barriers to adherence. A systematic review of randomized controlled trials that examined the impact of pharmacist interventions on osteoporosis management found that pharmacists may improve bone mineral density testing and calcium intake.[4] The authors note, however, that none of the interventions examined treatment adherence. A more recent study of 13 Dutch community pharmacies found that pharmacists can decrease nonadherence with and discontinuation of osteoporosis medication through counseling sessions and monitoring of drug use.[5] Additionally, a randomized controlled trial reported an increase in adherence for the pharmacist intervention group but no difference in persistence with osteoporosis medications.[6] None of these studies examined the impact on fractures. In this study, we evaluate the impact of an outpatient pharmacy clinical service (OPCS) program on patient medication adherence and fractures among patients with osteoporosis.

Methods

Description of the Outpatient Pharmacy Clinical Services Program

The Outpatient Pharmacy Clinical Services (OPCS) program incorporates quality clinical services within the daily outpatient pharmacy workflow at Kaiser Permanente. The program focuses on improving medication adherence, safety and clinical outcomes among members with chronic diseases. Pharmacists provide face-to-face consultations that focus on medication adherence during patient visits to the outpatient pharmacy. A previous study has demonstrated the effectiveness of the OPCS program in improving medication adherence and clinical outcomes among patients with diabetes and dyslipidemia.[7]

To impact adherence to osteoporosis drugs and reduce fractures, a pilot program has been started at Kaiser Permanente Orange County (KPOC), California. Outpatient pharmacists engage members picking up their first prescribed osteoporosis prescription in an expanded B-SMART (Barriers, Solutions, Motivation, Adherence Tools, Relationships, and Triage) consultation, which has been described in previous studies.[8,9] In short, the B-SMART methodology is a multifaceted approach used by the OPCS pharmacists to help patients more effectively use their medications. Pharmacists use a checklist during the consultation to confirm: 1) benefits of treatment to prevent fractures and improve bone strength, 2) proper use of prescribed medications and importance of adherence, 3) the need to refill the prescription in a timely manner before running out, 4) importance of daily intake of calcium and vitamin D, including a proper diet, 5) benefit of regular weight-bearing and muscle-building exercise, 6) smoking cessation, and 7) home hazard proofing to minimize fracture risks. A crucial aspect of the consultation is that OPCS pharmacists address potential common barriers that contribute to drug nonadherence and discuss patient-specific solutions with each patient. Common identified barriers include forgetfulness, side effects, denial of condition, financial challenges, a lack of social support, complex medication regimens and poor health literacy. To support patients in better drug adherence and in being successful in the management of osteoporosis, pharmacists triage patients with concerns regarding their osteoporosis treatment to health education classes, smoking cessation classes, or to their primary care physician to have further discussions. Pharmacists document their consultations for data gathering and subsequent analysis.

Prior to providing OPCS osteoporosis consultations, pharmacists participate in 3.5 hours of online and face-to-face training. The training includes osteoporosis clinical management review and related clinical competency, training on the B-SMART consultation methodology that incorporates motivational interviewing, and workflow training to optimize the integration of OPCS osteoporosis consultations within existing outpatient workflow.

Identification of Study Cohort

The setting for this study was the KPOC service area, which provides care to approximately 530,000 members. We used a retrospective database analysis that compared patients who received OPCS consultations to similar patients from KPOC who did not receive an OPCS consultation (usual care). A list of medical record numbers for consulted patients identified the OPCS group. To be entered into the cohort, patients were required to have at least one prescription for an osteoporosis-related medication from January 1, 2012, through December 31, 2013. Initial medications included oral and nasal forms of alendronate, calcitonin, etidronate, ibandronate, raloxifene, and risedronate. We excluded patients with a diagnosis of cancer, Paget's disease, or who were in hospice care. For the OPCS group, the index date was defined as the first consultation from January 1, 2012, through December 31, 2013, and for the usual care group, the index date was defined as the date of the first osteoporosis medication during the same time period. We included patients who were 18 years of age or older and had continuous health plan enrollment and a drug benefit for one year before and after the index date. Patients in the OPCS group were then matched to three patients in the usual care group based on patient age, gender and whether or not they had a previous medication for osteoporosis within six months before the index date. Patients were followed for one year after the index date. For the follow-up period, we included the same types of medications as the index medications, plus any injectables or infusions such as denosumab, teriparatide, pamidronate or zoledronic acid.

Outcomes

Our primary outcome was adherence to osteoporosis medications one year after the index date and was defined as having a medication possession ratio (MPR) ≥ 0.80. The MPR was calculated as the sum of the days of medication supply divided by the number of days between the first fill and last refill plus the days' supply of the last refill. The average time from the index date to the first prescription fill after the index date was analyzed, and the percent of patients with a timely fill was compared. If the first prescription after the index date was filled within 30 days after the end of the days' supply of the index prescription, then it was considered a timely fill. The percent of patients who discontinued their osteoporosis medications was also compared. We used a 30-day gap to determine timely fill as well as discontinuation. If there was no refill after the index date or if a gap of 30 days or more occurred during the study period, then it was considered discontinued. Finally, we compared the proportion of patients in each group who had only one fill of an osteoporosis medication.

The secondary outcome was whether or not the patient had a fracture one year after the index date. Fractures were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) principal diagnosis codes from any inpatient or outpatient data source. We included pathological fracture (733.1x), stress fracture (733.93, 733.94, 733.95, 733.96, 733.97, 733.98), spinal fracture (805.x, 806.x, 807.x, 808.x, 809.x), and fracture of the upper limb (810.x-819.x) and lower limb (820.x-828.x).

Statistical Analysis

Comparisons between the OPCS program and usual care were made using Pearson chi-square tests for differences in percentages and t-tests for differences in means. Baseline characteristics such as age and gender were compared between the OPCS and usual care groups. To ensure that patients were similar at baseline, we compared the average Charlson Comorbidity Index (CCI), which is a measure of comorbidity and includes patient encounter-based indicators for a variety of chronic conditions, including coronary heart disease, heart failure, diabetes and hypertension, as well as potentially life-threatening conditions such as AIDS, kidney disease, and liver disease.[10] Higher scores denote a greater number of severe comorbid conditions. A two-tailed P value of 0.05 was used to determine statistical significance. Using the primary outcome of adherence (percent of patients with an MPR ≥ 0.80), we estimated that we would need about 362 patients in each group (OPCS and usual care) to detect a 10 percent difference in adherence at 80 percent power and an alpha level of 0.05.

Multivariate analysis of the effect of OPCS consults on medication adherence was conducted using logistic regression. Covariates included age, gender, CCI, prior fracture, and prior use of osteoporosis medications. Logistic regression was also used to explore the risk of fracture, controlling for the same covariates, plus a measure of adherence to osteoporosis medications six months prior to the index date. We also conducted subgroup analyses among those patients who were new users (no prescriptions for an osteoporosis medication six months before the index date) and those who had previously used osteoporosis medications. Based on the logistic regression results, we reported patient characteristics associated with adherence and risk of fracture. All analyses were conducted using SAS 9.2 (SAS Institute Inc., Cary, North Carolina). The Institutional Review Board of KPSC approved this study.

Results

There were 1,172 patients in the OPCS group and 6,426 in the usual care group after inclusion and exclusion criteria were applied. We then matched one OPCS patient to three usual care patients based on age, gender and whether patients were either new or prior users, which resulted in 1,172 OPCS and 3,302 usual care patients in the final study cohort. There were 878 OPCS and 2,433 usual care new users and 294 OPCS and 869 usual care prior users. After matching, there were no significant differences between the two groups at baseline (Table 1). Most patients were female (80%), and their ages ranged from 37 to 98 years (mean = 72 years).

Descriptive analyses shown in Table 1 indicate that the OPCS group was more likely to have a timely first fill after the index date compared to the usual care group (74.2% vs. 70.5%, p = 0.039). There were no other significant differences for medication adherence in the full cohort. However, among patients who were new users of osteoporosis medications, the OPCS group was significantly more likely to be adherent one year after the index date (37.7% vs 32.8%, p = 0.009), have a higher average MPR (0.75 vs. 0.72, p = 0.011), fewer days to first fill after index (108 vs. 117, p = 0.01), and a timely first fill (74.5% vs. 65.4, p < 0.001) compared to the usual care group. OPCS patients also had a longer mean days of therapy (196 vs. 177, p = 0.001) and were less likely to discontinue their osteoporosis medications (72.8% vs. 77.7%, p = 0.003). Among prior users, usual care was favored in some of the adherence measures. Compared to usual care, OPCS prior users were less likely to have a timely first fill (73.6% vs. 81.1%, p = 0.011), shorter mean days of therapy (240 vs. 274, p = 0.001), more likely to discontinue their medications (58.5% vs. 51.1%, p = 0.028) and more likely to have only one fill (12.2% vs. 7.6%, p = 0.015).

Multivariate analysis of the full cohort showed no significant difference in drug adherence between OPCS and usual care patients (Table 2). Among new users, the OPCS group was significantly more likely to be medication adherent compared to the usual care group (OR = 1.23; 95% CI 1.05 – 1.44; p =0.012),

but this finding did not occur among prior users where the difference was not significant. Patient characteristics associated with adherence included male gender and lower CCI scores for both the full and new user cohort and prior fracture for the new user cohort, and, in the full cohort, prior users of osteoporosis medications were also significantly more likely to be adherent in the year after the index date compared to new users.

We found no significant differences between the OPCS and usual care groups in the percent of patients who had a fracture (Table 1) or in the risk of fracture (Table 2). In the full cohort, older age and having a prior fracture were significantly associated with an increased risk of fracture. Patients who were adherent to their osteoporosis medications were at reduced risk of fracture. The same patterns occurred in the new user cohort. Among prior users, only prior fracture was significantly associated with an increased risk of fracture.

Discussion

Results from this study show that the OPCS program was most effective among new users of osteoporosis medications. We found that 38% were adherent one year after the OPCS consultation, compared to 33% in the usual care group, and this effect held after controlling for covariates (OR 1.23; 95% CI 1.05-1.44). The OPCS program also improved the time to first fill and discontinuation rates. Among prior users, however, we found some favorable results for usual care, including a reduction in time to first fill and discontinuation, and an increase in mean days of therapy. Why would prior users in the usual care group have these improvements? A post-hoc analysis revealed that 9% of the OPCS group switched from oral alendronate to calcitonin nasal spray, compared to 1% of the usual care group ($p< 0.001$). Studies have shown reduced adherence with this medication, and one possibility is that we found a similar pattern in the OPCS patients.[11, 12] Future studies should be designed to identify which differences in drug type and dosing have the greatest impact on improved adherence.

Our results are similar to two previous studies. The MeMO program was composed of tailored counseling sessions by pharmacists and continuous monitoring of patients initiating osteoporosis medications.[5] They found that 19% of patients in the MeMO program discontinued their medications or were nonadherent, compared to 32.8% in the usual care group. While it is difficult to directly compare these measures to ours, it appears that their rates of medication discontinuation and nonadherence were lower than what we found. Their program included continuous monitoring, which has not been incorporated into our pilot program. A randomized controlled trial among new users of osteoporosis medications found a higher rate of adherence for the pharmaceutical care group compared to a control group (98% vs 96%; $p = 0.047$).[6] These high rates of adherence may be due to the method of assessing adherence (self-reporting), continuous monitoring, and the rigorous experimental setting. While our observational study depicts a more practice-based scenario that reflects real-world clinical care and patient behavior, continuous monitoring may be necessary to improve adherence in the long run.

We found no significant differences in fracture rates between the OPCS group and the usual care group. The sample size may have been too small to adequately detect fracture outcomes. Alternatively, patients were followed for one year, which may not be long enough to detect any significant difference in this important clinical outcome.

Limitations

Because patients were not randomized to the OPCS group versus the usual care group, it is possible that the results were attributable to systematic bias introduced by selection into the usual care group versus the OPCS group or that the two groups differed in other ways, such as socioeconomic status or educational levels, which may have affected patients' ability to adhere to their medications. Although the two groups were similar at baseline, a limited number of baseline factors were included, and we did not employ additional methods such as propensity scoring to further control for potential confounding. Nonpharmacological factors that could act as confounders were not assessed. This could include physical activity, diet, BMI, smoking and family history.

Conclusion

In summary, outpatient pharmacists are in a strategically excellent position to implement case management strategies to improve suboptimal medication adherence among patients with osteoporosis. By engaging patients with a new osteoporosis medication during a face-to-face consult, the OPCS pharmacist was able to influence and improve medication adherence.

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Table 1. Baseline characteristics, adherence and fractures of patients consulted by Outpatient Pharmacy Clinical Services (OPCS) compared to usual care patients. Mean ± standard deviation and column percentages reported.

	Full Cohort			New Users[a]			Prior Users[b]		
	OPCS N = 1,172	Usual Care N = 3,302	p-value	OPCS N = 878	Usual Care N = 2,433	p-value	OPCS N = 294	Usual Care N = 869	p-value
Baseline Characteristics									
Age, years	72±10.2	72±9.9	0.967	72.5±10.1	72.5±9.7	0.999	72.5±10.4	72.6±10.4	0.942
Female	934 (79.7%)	2,658 (80.5%)	0.552	696 (79.3%)	1,952 (80.2%)	0.543	238 (81.0%)	706 (81.2%)	0.912
Charlson Comorbidity Index	0.76±1.2	0.81±1.3	0.276	0.75±1.2	0.80±1.3	0.248	0.81±1.4	0.83±1.4	0.834
Prior Fracture	149 (12.7%)	453 (13.7%)	0.386	121 (13.7%)	387 (15.9%)	0.134	28 (9.5%)	66 (7.6%)	0.294
Prior Users[b]	294 (25.1%)	869 (26.3%)	0.409						
Adherence Measures									
Adherent	505 (43.1%)	1,353 (41.0%)	0.207	331 (37.7%)	799 (32.8%)	0.009	174 (59.2%)	554 (63.8%)	0.162
MPR	0.77±0.2	0.76±0.2	0.118	0.75±0.3	0.72±0.3	0.011	0.82±0.20	0.83±0.19	0.396
Days to first fill after index	105±64.9	110±65.2	0.092	108±69.8	117±73.2	0.010	101±51.8	96±41.5	0.153
Timely first fill	633 (74.2%)	1,735 (70.5%)	0.039	443 (74.5%)	1,084 (65.4%)	<.001	190 (73.6%)	651 (81.1%)	0.011
Mean days of therapy	207.3±146.6	202.9±146.7	0.379	196.0±142.8	177.3±137.5	0.001	240.9±152.6	274.5±147.9	0.001
Discontinued	811 (69.2%)	2,334 (70.7%)	0.339	639 (72.8%)	1,890 (77.7%)	0.003	172 (58.5%)	444 (51.1%)	0.028
One fill only	318 (27.1%)	841 (25.5%)	0.264	282 (32.1%)	775 (31.8%)	0.886	36 (12.2%)	66 (7.6%)	0.015
Fractures									
Any Fracture	95 (8.1%)	296 (9.0%)	0.371	76 (8.7%)	233 (9.5%)	0.422	19 (6.5%)	63 (7.3%)	0.649

[a]Patients without any osteoporosis medications 6 months before index date. [b]Patients with osteoporosis medications 6 months before index date. MPR = Medication Possession Ratio.

Table 2. Multivariate results for adherence[a] to osteoporosis medications and risk of fracture one year after index date.

	Full Cohort			New Users[b]			Prior Users[c]		
	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Adherence									
OCPS	1.11	0.96-1.27	0.153	1.23	1.05-1.44	0.012	0.83	0.63-1.09	0.174
Age	0.99	0.99-1.00	0.404	0.99	0.99-1.00	0.090	1.00	0.99-1.02	0.258
Male	1.37	1.17-1.59	<.001	1.48	1.24-1.77	<.001	1.07	0.79-1.46	0.660
Prior Fracture	0.90	0.75-1.09	0.277	0.98	0.80-1.20	0.849	0.64	0.42-0.99	0.042
Charlson Comorbidity Index	0.93	0.88-0.98	0.004	0.93	0.87-0.99	0.017	0.93	0.85-1.02	0.106
Prior User	3.26	2.83-3.75	<.001						
Risk of Fracture									
OPCS	0.93	0.73-1.19	0.561	0.96	0.73-1.27	0.781	0.84	0.49-1.44	0.521
Age	1.02	1.01-1.03	0.004	1.02	1.00-1.03	0.009	1.01	0.99-1.04	0.255
Male	0.77	0.57-1.02	0.067	0.79	0.57-1.09	0.157	0.67	0.36-1.27	0.220
Prior Fracture	4.86	3.86-6.11	<.001	5.11	3.96-6.58	<.001	4.01	2.27-7.09	<.001
Charlson Comorbidity Index	1.05	0.97-1.14	0.204	1.00	0.91-1.10	0.952	1.19	1.04-1.38	0.015
Adherent	0.77	0.61-0.97	0.029	0.74	0.56-0.96	0.026	0.88	0.55-1.40	0.581
Prior User	0.93	0.71-1.21	0.586						

[a]Adherence defined as having medication possession ratio of 80% or greater. [b]Patients without any osteoporosis medications 6 months before index date. [c]Patients with osteoporosis medications 6 months before index date. OPCS = Outpatient Pharmacy Clinical Services; CI = Confidence Interval.

[a]Patients without any osteoporosis medications 6 months before index date. [b]Patients with osteoporosis medications 6 months before index date. cPatients with osteoporosis medications 6 months before index date. OPCS = Outpatient Pharmacy Clinical Services; CI = Confidence Interval.