Utilization of Pharmacy Claims Data to Evaluate Therapeutic Interchange Programs

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OBJECTIVE: To gain insight into the accuracy of dosing guidelines and the overall success of a therapeutic interchange program by analyzing pharmacy claims data.

DESIGN: Evaluation of prescribing patterns via retrospective analysis of pharmacy claims data for therapeutic interchange between angiotensin II converting enzyme inhibitors (ACEIs).

SETTING: A California IPA-model HMO.

MAIN OUTCOME MEASURES: Percentage of conversion doses that corresponded with pharmacy and therapeutics (P&T) guidelines, variation among actual conversion doses utilized, and number of dosage titrations associated with implementing conversions.

RESULTS: The analysis revealed that dosing ratios utilized to convert patients from lisinopril, quinapril, enalapril, and ramipril to benazepril HCl corresponded with P&T guidelines 83%, 78%, 54%, and 26% of the time, respectively. The variance in conversion doses from

enalapril and ramipril was significantly greater than from lisinopril and quinapril ($p < 0.01$). The overall percentage of patients experiencing a dosage titration was low, 3.8%, but somewhat higher for patients converted specifically from ramipril (9.4%).

CONCLUSIONS: Conversion dosages were most consistent between products with similar tablet strengths, the same recommended starting doses, and a high volume of use. The rate of dosage titrations in this therapeutic interchange program was low, indicating a high probability of success. Similar analysis can be used to alert P&T committees to the difficulty or simplicity associated with converting patients during future therapeutic interchange programs, and to assess the accuracy of their dosing guidelines.

KEYWORDS: Angiotensin converting enzyme inhibitors, ACEI, Therapeutic interchange, Pharmacy claims, Automated data

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Clinical circumstances and economic pressures often lead pharmacy and therapeutic (P&T) committees to develop and implement therapeutic interchange programs. Such programs can be cost-effective tools for managing pharmacy expenditures or for converting patients to a new product that may have superior clinical benefits. P&T committees must also educate providers about the benefits of the preferred agent and provide recommendations for making drug conversions, often through guidelines developed to assist providers in making dosage selections. However, without randomized controlled studies on dose equivalence, knowing if the guidelines P&T committees provide are accurate, or if they will be followed, is difficult.

In one therapeutic interchange program between fluoxetine and sertraline, the P&T committee provided inaccurate information on dose equivalence, which contributed to the failure of the program. Review of patient charts found that of 24 patients converted from 20 mg of fluoxetine, 10 patients were maintained on sertraline 50 mg/day, seven required 100 mg/day, four required 150 mg/day, and three required 200 mg/day, when the recommended conversion dose was 50 mg/day. Researchers concluded that the information available on dose equivalence was inadequate and not pertinent to therapeutic interchange, and that future policies should be evaluated systematically and prospectively whenever possible.¹

Many other therapeutic interchange programs have been successful, such as the one at Grady Health System,² where a voluntary therapeutic interchange protocol resulting in 1,500

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conversions between angiotensin II converting enzyme inhibitors (ACEIs) over a two-year period was expected to save the organization \$259,054. Similar studies also have shown that the magnitude of net savings achieved through therapeutic interchanges is significantly affected by the costs associated with the conversion, which may include additional clinic visits, labs, or new prescriptions. Further, these studies show that as the use of these resources increases, the length of time before the health system realizes net savings also increases.^{3,4} In younger, uncomplicated patients, these costs can be reduced if guidelines help providers select the best conversion dosage or discourage physicians from making all conversions to the lowest recommended starting dose of the new medication, and then titrating upward for the desired effect.

The Health Plan of the Redwoods (HPR) in Northern California responded to the economic pressure of increasing pharmacy expenditures by implementing a therapeutic interchange program between ACEIs. Before initiating this program, the P&T committee developed dosing guidelines based on drug manufacturers' starting dose recommendations (see Table 1). In analyzing this program, the authors describe a simple methodology for comparing actual conversion doses utilized to that of guideline recommendations. We also compare rates of dosage titrations and discuss the findings as they pertain to the conduct and evaluation of future therapeutic interchange programs.

METHODOLOGY

Sample population

Potential study candidates were identified from automated ACEI prescription claims. These records were extracted from prescription claims tapes and imported to an Access database in which selection criteria were used to identify study members with a high probability of being part of the therapeutic interchange process. Three inclusion criteria were used:

▲ The patient's electronic prescription record was required to contain a claim for both benazepril HCl and one of the other ACEIs involved in the therapeutic interchange process—lisinopril, quinapril, enalapril, or ramipril.

▲ The switch date for the new prescription claim had to

Table 1. P&T Conversion Guidelines

	Package Insert Starting Dose	Dose Conversion Guide			
Benazepril HCl	10 mg	5 mg	10 mg	20 mg	40 mg
Lisinopril	10 mg	5 mg	10 mg	20 mg	40 mg
Quinapril	10 mg	5 mg	10 mg	20 mg	40 mg
Ramipril	2.5 mg	2.5 mg	5 mg	10 mg	20 mg
Enalapril	5 mg	5 mg	10 mg	20 mg	40 mg

appear during the period June 1996–September 1996, the time during which the therapeutic interchange program was being conducted and guidelines were in effect.

▲ The number of days elapsed between the dates of the interchanged ACEIs had to be less than 30, plus the days supply indicated in the preswitch medication claim. This eliminated patients with long gaps in treatment, which is indicative of stopping and restarting therapy rather than converting.

After identifying patients involved in the therapeutic interchange program, we excluded patients if their pharmacy records did not contain two identical and consecutive dosages for the preswitch medication. This step, which eliminated patients who had not stabilized on their antihypertensive medication prior to conversion, was introduced to minimize the chance of deviation from guidelines for clinical reasons. This requirement was dropped for patients converted from enalapril to maintain the sample size.

Calculation of Dosing Ratios

The dosing ratio used to convert each patient between products was calculated from the pharmacy claim by dividing the total daily dose of the post-switch medication by the total daily dose of the preswitch medication. For example, if a patient was converted from 10 mg of product A to 10 mg of product B, he or she was given a dosing ratio of 1. If the ending medication dosage was one-half or one-fourth of the starting medication dosage, the dosing ratio would be scored as 0.5 or 0.25, respectively. Those doses that were doubled or quadrupled received dosing ratios of 2 or 4.

To determine a patient's total daily dose of medication, the following data elements were used: medication strength; quantity dispensed (number of tablets); and days supply. The number of doses consumed by the patient each day was calculated by dividing the quantity dispensed by the days supply. For example, if 60 tablets were dispensed as a 30-day supply of medication, then the number of daily doses consumed would be two. A total daily dosage was then computed by multiplying the strength of the medication dispensed by the number of doses consumed each day (see Table 2).

In relatively few cases, daily consumption rates resulted in a number that did not exactly indicate a once- or twice-daily dosing regimen. For these patients, the resulting fraction was rounded to the nearest whole number that was indicative of a clinically meaningful dosing regimen. Because the ACEIs involved in this analysis should all be dosed either once or twice daily, this strategy for dealing with less-than-perfect claims was both simple and straightforward.

Dosage Titrations and Conversion Patterns

Potential dose titrations were tracked for 90 days after the conversion. If during this time a patient obtained a prescription with a total daily dose different from that of the original conversion dose, he or she was identified as having a dose titration.

To make comparisons between actual conversion doses

Table 2. Calculation of Total Daily Doses

Prescription Data from Pharmacy Claims				Calculated Data	
Drug	Strength	Quantity Dispensed	Days Supply	Daily Consumption Rate	Total Daily Dose
A	10 mg	60	30	2 (60/30)	20 mg (10 mg x2)
B	20 mg	30	30	1 (30/30)	20mg (10 mg x1)

utilized and those of guideline recommendations, dosing ratios were grouped by the preswitch medication from which the patients were converted. Because all study members were converted to the same agent, benazepril HCl, this was used as the reference medication for making comparisons between groups. Descriptive statistics (medians, means, and standard deviations) were performed on each group of conversions, and the variance in dosing ratios between medication groups was tested for significance using the F-test. For each group of conversions, the number of patients with a dosage titration after the conversion had occurred was tabulated to serve as a proxy for the amount of "excess" medical resource consumed in making the conversions.

FINDINGS

A total of 453 ACEI conversions were analyzed. Of these, 33, 53, 127, and 240 were conversions from enalapril, ramipril, quinapril, and lisinopril to benazepril HCl, respectively. The percentages of therapeutic interchange doses that correlated with guideline recommendations are presented in Table 3. Overall, 70.2% of these conversions corresponded with guideline recommendations. For patients converted specifically from enalapril and ramipril, the percentages of conversions corresponding with guideline recommendations were somewhat lower—54% for enalapril and 26% for ramipril. The overall percentage of patients who had a dosage titration was also low, 3.8%, and ranged from 3.0% to 9.4% for conversions from enalapril and ramipril, respectively.

DISCUSSION

Table 4 shows the mean, median, and standard deviation for dosing ratios associated with each group of conversions. For each group the average dosing ratio utilized was slightly higher than that of the guideline recommendations. The presence of higher-ending conversion dosages might imply that some conversions were made to gain better blood pressure control by increasing the dosage of the new medication. However, absence of blood pressure measures prevents confirmation that the increases in conversion doses were manifestations of poor blood pressure control. (Determining whether the skew in dosing ratio averages would be reduced or eliminated

by merging each group of conversions with an equal number of conversions in the opposite direction under the same conditions would be interesting.)

The standard deviation for each group of dosing ratios was highest in the enalapril and ramipril groups, 1.00 and 1.32, respectively, and the variance found in these conversions was significantly greater than that of the lisinopril and quinapril groups ($p < 0.01$ F-test).

The difference in variation might be explained by characteristics of the medications. Three products—benazepril HCl, lisinopril, and quinapril—have similar strengths available on the market, including 5, 10, 20, and 40 mg tablets. Also, the manufacturers' recommended starting dose for lisinopril and quinapril is 10 mg, the same recommended starting dose as that for benazepril HCl. Because of these product similarities, providers might assume patients to be equally responsive to these drugs. The other ACEIs studied lack these basic similarities. Both enalapril and ramipril have lower recommended starting doses, 5 mg and 2.5 mg, respectively, and ramipril is marketed in much lower tablet strengths (1.25, 2.5, 5, and 10 mg) than benazepril HCl. This relative lack of similarity between these products may reduce providers' ability to predict dose responsiveness, thus increasing the expected variability in dosing ratios with these agents.

Variation in dosing ratios also might have been affected by the amount of clinical experience that providers had with each of the products. Dosing ratios were most consistent in the lisinopril and quinapril groups, which were also the products with the highest utilization. Because they have had more clinical experience with these products, perhaps clinicians can better predict dose responses.

The overall percentage of patients having a dosage titration (3.8%) was very small for this therapeutic interchange program. While electronic data were not available on the number of followup visits associated with the conversion dosage titrations likely indicate consumption of some type of "excess" medical resources, such as an additional office visit to recheck blood pressure, or a phone call with a provider regarding the management of a side effect. Patients converted from ramipril to benazepril HCl had the highest percentage of dosage titration (9.4%). Assuming that these titrations were in fact associated

Table 3. Summary of Findings

Conversion Pair	% of Conversions Corresponding to Guidelines	% of Conversions That Contained a Dose Titration
Lisinopril to benazepril HCl	83%	3.3%
Quinapril to benazepril HCl	78%	3.9%
Enalapril to benazepril HCl	54%	3.0%
Ramipril to benazepril HCl	26%	9.4%
All conversions to benazepril HCl	70.2%	3.75%

with the use of additional medical resources, the marginal economic benefit of converting patients from ramipril to benazepril HCl should be less, relative to the other products involved in the therapeutic interchange program. Other products had rates of dosage titration between 3% and 4%, indicating minimal use of "excess" medical resources.

Implication of Findings

Other research has shown that pharmacy claims data can be a useful tool for monitoring patient compliance with drug therapy.⁵ Similarly, this analysis demonstrates how pharmacy claims can be used to gain insight into the difficulty or ease of converting patients between specific products. Using this methodology, large volumes of pharmacy data can be evaluated quickly, and at considerably less cost than chart review methods.

In medication classes such as ACEIs, where safety and effectiveness have been shown to be equivalent,⁶ therapeutic interchanges likely will continue to be implemented for cost containment. The variation measured in each group of conversion dosages is of interest because this variation may indicate confusion among providers. Without prospective clinical trial data on dose equivalence, retrospective analysis can provide valuable information. This study showed that conversion dosages between products with similar tablet characteristics and a high volume of use were the most consistent. These findings suggest that nonclinical variables, such as tablet strengths and volume of use, should perhaps be considered when all other clinical and economic features of drug products are the same.

The rate of dosage titrations also provides insight regarding the overall success of a therapeutic interchange program. Had investigators evaluated the fluoxetine/sertraline interchange program with this methodology, they would have found a dosage titration rate of 68% (14 out of 24 patients with a titration). This finding could have alerted the P&T committee to difficulties in the program and enabled them to stop the program or to modify guidelines.

LIMITATIONS

One limitation of this methodology is the lack of clinical measures. Without clinical data, a determination of whether dosage titrations or the variation found in dosing ratios was associated with a lack of blood pressure control cannot be made. Our methodology selected for patients involved in the therapeutic interchange process, which means the drug conversions should have been made for formulary reasons only. However, clinical events, such as side effects or poor blood pressure control, could have been present during the interchange process, contributing to differences found in conversion doses and rates of dosage titration.

The use of pharmacy claims data says nothing about the actual consumption of the medication by the patient. Whether the conversion dosages calculated from the claims are representative of how providers actually directed their patients to

Table 4. Descriptive Statistics

Conversion Group	Recommended Dosing Ratio by Guidelines	Median Dosing Ratio Practiced	Average Dosing Ratio Practiced	SD of Dosing Ratios
Lisinopril to benazepril HCl	1	1	1.07	.43
Quinapril to benazepril HCl	1	1	1.05	.44
Ramipril to benazepril HCl	2	2	2.19	1.32
Enalapril to benazepril HCl	1	1	1.65	1.00

take medication is unknown. If, for example, a patient received a prescription for 10 mg, but was directed by the physician to increase the dose from one tablet to two tablets after the first week of treatment, this change would go undetected in the pharmacy claims database. Likewise, this study did not account for differences that may have existed in compliance behavior. If a patient became more or less compliant after switching medications, dosage adjustments might be required that should not be attributed to the interchange process.

Utilization of pharmacy claims data proved to be a quick and simple tool for evaluating a therapeutic interchange program. Conversion doses were most consistent between products with similar tablet strengths, the same recommended starting doses, and a high volume of use. The rate of dosage titrations in this therapeutic interchange program was low, indicating a high probability of success. Similar analysis can be used to alert P&T committees to the difficulty or simplicity of converting patients during future therapeutic interchange programs, and to assess the accuracy of dosing guidelines.

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