Outcome Analysis of a Formulary Transition from Nifedipine to Felodipine at a Veterans Affairs Medical Center

Alfreda L. Kinnon, Julian Bourne, Stephanie Blizzard, Dee Hunter, and Cynthia Phillips

OBJECTIVE: To perform an efficacy outcome and cost analysis and to assess the risk factors of patients converted from nifedipine extended-release tablets to felodipine extended-release tablets.

DESIGN: A retrospective chart review analysis of patients who underwent a mandated formulary switch between 1/94 and 12/96.

SETTING: The William Jennings Bryan Dorn Veterans Affairs Medical Center (VAMC), Columbia, SC, ambulatory care clinics.

PATIENTS: 230 hypertensive patients enrolled in outpatient ambulatory clinics.

MAIN OUTCOME MEASURES: Pre- and post-conversion blood pressure and heart rate measurements, adverse events, and concomitant antihypertensive therapy used before and after the formulary switch was determined. A comparative cost analysis of the dihydropyridines used in the switch was conducted. The prevalence of comorbidity risk factors was assessed.

RESULTS: Blood pressure control, heart rate, and the number of patients controlled to diastolic blood pressure DBP<90mm Hg was similar for all patients pre- and post-dihydropyridine conversion. A greater number of white patients was controlled to DBP<90mm Hg in contrast to the black patient population. Adverse events and additional antihypertensive medications prescribed were similar before and after the conversion. The monthly cost savings for these patients converted to felodipine was substantial.

CONCLUSIONS: The VA formulary dihydropyridine conversion resulted in post-conversion felodipine blood pressure and heart rate control in all patients reviewed that were similar to that of preconversion nifedipine blood pressure and heart rate control. This switch proved to be a cost-effective addition to our formulary.

KEYWORDS: Nifedipine, Felodipine, Cost, Formulary, Comparative, Outcome, Blood pressure, Dihydropyridine

J Managed Care Pharm 1999:425-428

The delivery of quality health care at reduced cost is an essential objective for the maintenance of institutional provider organizations. Health care services are provided in growing numbers on an outpatient basis, especially in Veterans Affairs Medical Centers (VAMCs). Minimizing prescription cost expenditures would prove beneficial to institutional pharmacies. The conversion from the extended-release dihydropyridine calcium channel blocker nifedipine to the extended-release dihydropyridine calcium channel blocker felodipine has resulted in substantial cost savings for other institutions.1,3

Both formulations have demonstrated significant antihypertensive efficacy while affording once-daily dosing.1,3 A retrospective outcome analysis of patients converted from nifedipine to felodipine at a VAMC was conducted to assess blood pressure control, heart rate, adverse effects, and cost of therapy both preceding and succeeding the switch. The results of this and other similar studies can be utilized to select dihydropyridine calcium channel blockers for the management of hypertension.1,4

METHODS

Patient Population

This study considered 230 ambulatory care patients who received a prescription change from nifedipine extended release to felodipine extended release between January 1994 and December 1996. Prior to the formulary change, clinical pharmacists educated providers of ambulatory care about the institutional
decision to replace nifedipine with felodipine ER unless indications warranted substitution of the more expensive dihydropyridine, amlodipine. Treatment with amlodipine was recommended for patients with left ventricular dysfunction (LVEF<40%) who experienced recurrent failure despite maximal treatment with digoxin, diuretics, angiotensin-converting enzyme inhibitors, and/or combination isosorbide dinitrate and hydralazine. Also included were those patients with frequent recurrences of angina despite use of beta blockers, nitrates, calcium antagonists (other than amlodipine), and aspirin.5,6

Dosing Conversion
All providers received a predefined dosage conversion scale researched and designed by the VAMC that represented daily dihydropyridine doses and recommended a follow-up algorithm for the management of hypertension. The scale recommended that patients on a total daily dose of 30 mg of nifedipine be switched to 2.5–5.0 mg of felodipine with follow-up in 2–4 weeks. If a patient had been taking nifedipine 60 mg, recommendations included switching to 5–10 mg daily of felodipine with follow-up in 2–4 weeks. Patients on 90 mg of nifedipine were converted directly to felodipine 10 mg daily with follow-up in 1–2 weeks. If adequate blood pressure was not achieved during follow-up, titration of felodipine from 2.5 mg to 5.0 mg or from 5 mg to 10 mg daily was recommended, with follow-up in 2–4 weeks. For those patients whose blood pressure was not controlled on 10 mg daily of felodipine for at least two weeks as determined during a follow-up visit, the addition of a second hypertensive agent was recommended with follow-up in 2–4 weeks.

Exclusion Criteria
Patients were excluded from the study if: 1) dihydropyridine was indicated for a condition other than hypertension; 2) the patient never actually received felodipine; 3) there was documented noncompliance with medication or follow-up appointments for blood pressure evaluation in patient records; or 4) no pre- or post-conversion blood pressure data were available.

Vital Signs Technique
Bianually calibrated digital vital sign monitors or handheld sphygmomanometers were used to obtain patient blood pressure. Blood pressure and heart rate were determined using standard techniques of examination. Ambulatory care physicians, midlevel practitioners (nurse practitioners or physician assistants), or clinical pharmacists performed blood pressure management duties both before and after the switch.

This study was presented to and approved by the VAMC Institutional Review Board. Following the institution of exclusion criteria, 157 patients were eligible to be evaluated for the analysis from the initial roster of 230 patients.

Study Design
Patient records and computer progress notes were reviewed to obtain preconversion and post-conversion blood pressure and heart rate measurements. Up to three of the most recent blood pressure and heart rate measurements following the final dosage titration of nifedipine before the transition to felodipine, and up to three subsequent blood pressure and heart rate measurements following the final dosage titration of felodipine, were recorded. Switch patients not scheduled for follow-up blood pressure and heart rate evaluation were scheduled for assessment with one of four clinical pharmacists. Adverse effects and concomitant antihypertensive medications were obtained from patient charts, computerized progress notes, and active medication profiles. A outcome analysis data form was created to indicate individual patient demographics, pre- and post-conversion dihydropyridine agent, blood pressure and heart rate measurements, concomitant blood pressure medications, and adverse events. A comorbidity risk factor assessment, including patient history of tobacco use, diabetes, hyperlipidemia, peripheral vascular disease, renal insufficiency or failure, and coronary artery disease, was conducted.

Cost Analysis
The analysis of cost compared direct expenses of the dihydropyridine agent only. The comparative therapeutic expense represented the VAMC acquisition cost to maintain 157 patients on nifedipine extended release for one month before conversion, compared to the post-conversion cost of felodipine for one month. The price per dispensed unit for one dose of nifedipine was $0.63 for 30 mg, $1.13 for 60 mg, and $1.16 for 90 mg. By comparison, felodipine price per dispense unit was $0.48 for 2.5 mg, 5.0 mg, or 10 mg. The cost of the dihydropyridine agent was based on the Federal Supply Schedule, which is utilized for government drug pricing determination.

Data Analysis
Blood pressure and heart rate values were averaged for up to three visits preconversion and post-conversion for each patient. The mean and standard deviation of systolic and diastolic blood pressure, as well as heart rates both preconversion and post-conversion, were determined. Continuous data were presented as the mean ± the standard deviation (SD). For all analyses, a level of significance for a two-tailed test of <0.05 was considered statistically significant.10,11

RESULTS
Demographic data evaluation indicated the average patient age was 63 years old ± 12 years. The population consisted of 153 males (97%) and four females (3%), with 79 white patients (50%) and 78 black patients (50%).

Before conversion, 67 patients were titrated to 30 mg nifedipine, 58 titrated to 60 mg nifedipine, and 32 patients titrated to 90 mg nifedipine. Following conversion, no patients were titrated to 2.5 mg felodipine, 80 patients were titrated to 5 mg felodipine, and 77 patients were titrated to 10 mg felodipine.

The average dose for a patient on preconversion nifedipine
Table 1. Blood Pressure and Heart Rates Before and After Conversion

<table>
<thead>
<tr>
<th>Nifedipine XL</th>
<th>Average Dose</th>
<th>Systolic BP</th>
<th>Diastolic BP</th>
<th>Heart Rate</th>
<th>Controlled to DBP&lt;90 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients (N=157)</td>
<td>53</td>
<td>147</td>
<td>80</td>
<td>80</td>
<td>131 (83)</td>
</tr>
<tr>
<td>White Patients (N=79)</td>
<td>51</td>
<td>147</td>
<td>78</td>
<td>81</td>
<td>69 (87)</td>
</tr>
<tr>
<td>Black Patients (N=78)</td>
<td>56</td>
<td>147</td>
<td>82</td>
<td>79</td>
<td>60 (77)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Felodipine ER</th>
<th>All Patients (N=157)</th>
<th>7.5</th>
<th>145</th>
<th>79</th>
<th>81</th>
<th>137 (87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Patients (N=79)</td>
<td>7.4</td>
<td>143</td>
<td>76</td>
<td>82</td>
<td>74 (94)</td>
<td></td>
</tr>
<tr>
<td>Black Patients (N=78)</td>
<td>7.5</td>
<td>148</td>
<td>81</td>
<td>79</td>
<td>61 (78)</td>
<td></td>
</tr>
</tbody>
</table>

was 53 mg ± 23 mg; for post-conversion felodipine the average dose was 7.5 mg ± 2.5 mg. Mean preconversion nifedipine and post-conversion felodipine systolic, diastolic, and heart rate of all patients are shown in Table 1. While on nifedipine, 131 patients (83%) were controlled to a diastolic blood pressure (DBP)<90 mm Hg. Following conversion to felodipine, 137 patients (87%) were controlled. This difference in control was of statistical significance (p<0.05). Compared to the black population before and after conversion, more white patients were controlled to a DBP<90 mm Hg. Before conversion to felodipine, 69 (87%) white patients were controlled on nifedipine.

Following conversion to felodipine, 74 (94%) patients were controlled. This improvement in blood pressure control was statistically significant. Sixty (77%) black patients were controlled on nifedipine while 61 (78%) were controlled on felodipine. This difference was not statistically significant.

Documented patient side effects attributed to the dihydropyridines included seven reports of edema on nifedipine and seven reports of edema once switched to felodipine. Four reports of headache while on nifedipine and four reports of headache following the transition to felodipine were reported. Also, two reports of erectile dysfunction, two reports of dizziness, one report of heartburn, and one report of sore gums were reported in felodipine-treated patients. In this study and other similar analyses, headache and edema were two of the most commonly reported side effects.

Concomitant medications prescribed to patients while on nifedipine or felodipine included diuretics, angiotensin converting enzyme (ACE) inhibitors, alpha-blockers, beta-blockers, and central alpha-1 agonists. There was no significant difference in those patients who were on these medications preconversion nifedipine vs. post-conversion felodipine.

Comorbidly often is associated with a modified disease state prognosis and negative impact on patient survival. In an elderly population, a single individual may have multiple chronic conditions. An analysis of our patient population revealed that 25% used tobacco, 31% were diabetic, 30% had hyperlipidemia, 8% had peripheral vascular disease, 24% had coronary artery disease, and 12% had renal insufficiency and/or failure.

An estimated monthly cost of $4,400 was required to maintain those patients on nifedipine, while $2,315 per month was the cost to treat these patients following conversion to felodipine—a difference of $2,085 dollars. When considered for the entire institution, the savings will prove to be quite substantial. This amount did not include adjunct antihypertensive medications utilized.

**DISCUSSION**

Numerous studies have demonstrated the efficacy, tolerability, and safety of dihydropyridine calcium channel blockers. Blood pressure and heart rates obtained from related analyses were similar to those found in this study (see Table 2). The results of this study confirm that dihydropyridine felodipine extended release provides control of blood pressure and heart rate comparable to nifedipine extended release. A DBP controlled to <90 mm Hg was indicated since the benefits of treatment for diastolic hypertension in older individuals have been firmly established. The control of elevated DBP is also associated with a reduction in cardiovascular and cerebrovascular events, as well as total mortality.

The felodipine post-conversion blood pressure control was improved in our white population. Sixty-nine (87%) patients were controlled to DBP<90 mm Hg on nifedipine; when converted to felodipine, 74 (94%) patients were controlled to the indicated level, following dose titration. However, no statistically significant improvement in blood pressure control was noted in the black population. When using nifedipine, 60 (77%) black patients were controlled to DBP<90 mm Hg; after conversion, only one additional patient (61, or 78% of the total population) was controlled. Our analysis was unique in that our study population was 50% black; in other analyses the proportion of black patients was 37% or less.

This was not a controlled study; therefore, there are associated limitations. Some patients used in the analysis were switched prior to the review period and therefore had fewer than three blood pressure or heart rate measurements available for evaluation. Due to our predominantly elderly male population,
which is representative of a VAMC, these results do not necessarily represent the general population.

CONCLUSION

In this era of reform, care delivery methods that produce satisfactory outcomes and reduce or maintain costs must be developed.15 Outcomes research is an effective evidence-based method of providing quality medical care. Research has demonstrated that the long-acting dihydropyridines such as nifedipine and felodipine are more effective in controlling blood pressure in older patients.16-18 This study sought to retrospectively evaluate outcomes of a formulary transition that occurred in the daily management of a VAMC patient population. Converting patients from nifedipine extended release to felodipine extended release resulted in significant cost savings for one month of drug therapy for 157 patients. In addition, preconversion and postconversion blood pressure control and heart rate were comparable to previous similar studies as indicated in Table 2.13

In this study population, which comprised primarily older patients with substantial comorbidity states, felodipine was shown to be as least as effective as nifedipine in controlling blood pressure; previously reported studies have reached the same conclusion.14 This analysis represented only a small segment of those patients converted. Once the cost savings are considered for the entire switched population, the utilization of felodipine as an alternative dihydropyridine will result in tremendous prescription expenditure savings.

Due to concerns associated with the rising cost of health care, drug efficacy and cost must be considered when making formulary decisions. When cost-containment strategies are utilized, associated possible adverse effects on patient quality of care must be avoided.19 Formulary conversion analyses can help provide effective antihypertensive control that is acceptable to the patient and the provider and will allow for the maintenance of our institutional provider organization.

References

17. Weinberger MH. The role of age, race, and plasma renin activity in influencing the blood pressure response to nitrendipine or hydrochlorothiazide. J Clinical Pharmacy 1987; 9 suppl 4: 272-75.