Evaluation of Blood Pressure and Adverse Effects in Patients Converted from Lisinopril to Benazepril

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OBJECTIVE: To compare blood pressure, serum creatinine, and serum potassium in stable patients before and after conversion from lisinopril to an equivalent dose of benazepril.

DESIGN: A retrospective analysis of computer medical and pharmacy records during a one-year period, to obtain the last measured blood pressure, serum creatinine, and serum potassium obtained while patients were receiving lisinopril and again after conversion to benazepril. Certain measurements were excluded to decrease the influence of factors others than the angiotensin converting enzyme (ACE) inhibitors.

SETTING: A Veterans Affairs Medical Center located in the western United States.

PATIENTS: 687 patients were evaluated for blood pressure; 433 for serum creatinine; and 422 for serum potassium. The patients were predominantly elderly males.

MAIN OUTCOME MEASURES: Measures of blood pressure, serum potassium and serum creatinine.

RESULTS: No statistical difference was found for systolic blood pressure, diastolic blood pressure, or serum potassium following conversion. There was a statistically significant decrease in levels of serum creatinine (1.199 vs. 1.172, p=0.007), but this decrease is probably not clinically significant.

CONCLUSION: Routine additional monitoring of blood pressure, serum potassium, and serum creatinine does not appear to be needed when converting patients from lisinopril to benazepril. The annual drug cost savings of this conversion totaled almost $50,000 at this medical center.

KEYWORDS: Blood pressure, Serum creatinine, Serum potassium, Conversion, ACE inhibitor

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While several angiotensin converting enzyme (ACE) inhibitors are commercially available, no compound appears to have clear advantages over any other. Thus, competitive pricing has provided the incentive to convert patients to the least expensive product. Although dose response studies suggest that the potencies and kinetics are very similar among the long-acting ACE inhibitors, direct comparative studies are not available. Conversion from one medication to another thus raises concerns about equivalent dosing, clinical response, and potential adverse effects.

Lindgren-Furmaga et al. have compared the total cost of switching hypertensive patients from enalapril maleate to an equal milligram dosage of lisinopril. In the group randomized to receive lisinopril (n=25), five patients (20%) required a double dose of lisinopril and one patient (4%) required a half-dose to maintain blood pressure control. In the group that continued to receive enalapril (n=21), two patients (9.5%) required a double dose to control blood pressure. Because the patients who converted from enalapril to lisinopril required more dosage adjustments to maintain control, the authors considered a follow-up visit advisable. They noted that the cost of additional follow-up visits would increase nondrug costs and should be considered when calculating the overall savings of switching from one ACE inhibitor to another.

McDonough et al. studied the economic impact of a voluntary switch program of lisinopril for enalapril in a staff model...
Table 1. Effects of Converting Patients from Lisinopril to Benazepril

<table>
<thead>
<tr>
<th>Parameter Measured</th>
<th>Drug</th>
<th>n</th>
<th>Mean ± SD</th>
<th>Paired Sample Difference in Means ± SD</th>
<th>95% Confidence Interval of the Difference in Paired Sample Means</th>
<th>p value (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>lisinopril/benazepril</td>
<td>687/687</td>
<td>139 ± 20 / 140 ± 22</td>
<td>-0.66 ± 21.8</td>
<td>(-2.29) - (0.97)</td>
<td>0.426 N.S.</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>lisinopril/benazepril</td>
<td>687/687</td>
<td>80 ± 12 / 80 ± 12</td>
<td>-0.31 ± 12.6</td>
<td>(-1.26) - (0.63)</td>
<td>0.517 N.S.</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>lisinopril/benazepril</td>
<td>433/433</td>
<td>1.2 ± 0.4 / 1.2 ± 0.4</td>
<td>-0.027 ± 0.21</td>
<td>(-0.047) - (-0.0074)</td>
<td>0.007</td>
</tr>
<tr>
<td>Serum potassium (mEq/L)</td>
<td>lisinopril/benazepril</td>
<td>422/422</td>
<td>4.4 ± 0.2 / 4.4 ± 0.5</td>
<td>0.046 ± 0.53</td>
<td>(-0.0045) - (0.097)</td>
<td>0.0793 N.S.</td>
</tr>
</tbody>
</table>

health maintenance organization (HMO). They compared the drug, laboratory, administrative, and clinical costs and the costs associated with adverse effects of 75 patients who were converted to lisinopril and 52 who remained on enalapril. Their study design precluded analysis of blood pressure control between groups. Compared to the control group, patients converted to lisinopril had more office visits over a 12-month period (4.54 vs. 2.6).

There was no difference in the number of laboratory tests between groups. Seven patients (9%) converted to lisinopril had mild adverse effects and were changed back. Although increased office visits, adverse effects, and administrative activities resulted in higher indirect costs, the lower drug acquisition cost generated an overall cost savings within the first year.

In 1994, our medical center changed the formulary ACE inhibitor from lisinopril to benazepril due to the latter's lower acquisition cost. Because no direct comparative trials were available, it was assumed that an equal daily dose conversion would be appropriate, based on individual dosing studies for these two drugs. After the Pharmacy & Therapeutics Committee approved the change, patients who presented new prescriptions for lisinopril automatically received an equivalent dosage of benazepril. We conducted this retrospective study to determine if patients who had received lisinopril maintained the same blood pressure, serum creatinine, and serum potassium after conversion to benazepril.

RESULTS

The patients studied were veterans receiving care at the Tucson Veterans Affairs Medical Center. Most were elderly males receiving ACE inhibitors, post-myocardial infarction, for treatment of diabetic nephropathy, hypertension, and congestive heart failure. The indication for treatment was not considered in the analysis.

In total, 1,288 patients were converted from lisinopril to benazepril. Of these patients, 932 (72%) were started on a dose of benazepril equal to the last dose of lisinopril. After excluding data inappropriate for analysis, 696 patients were found to have blood pressures appropriate for our analysis; 422 patients had serum potassium values that could be evaluated; and 433 patients had serum creatinine values suitable for analysis (see Table 1). No statistical difference was found for systolic blood pressure, diastolic blood pressure, or serum potassium following conversion from lisinopril to an equal daily dose of benazepril. There was, however, a statistically significant decrease in serum creatinine (1.199 vs. 1.172; p=0.007).
DISCUSSION

The clinical outcome of converting patients from one ACE inhibitor to another is unknown. Altered pharmacologic response and the possibility of adverse effects may dissuade practitioners from attempting a therapeutic exchange. In this large retrospective study, we found no difference in the mean blood pressure control or the incidence of hyperkalemia in patients switched from lisinopril to benazepril. The decrease in serum creatinine following the conversion to benazepril, though statistically significant, probably is not clinically significant, since the standard laboratory serum creatinine test is unable to accurately report levels smaller than 0.1 mg/dL. When comparing values reported by the lab in clinical practice, the difference probably would be undetectable. These results occurred in a population of patients being treated with ACE inhibitors for a variety of medical indications.

This study has several limitations due to its retrospective nature and lack of controls. Because of the extended study period, the influence of time or the addition or deletion of other medications may have affected the results. However, it is unlikely that other antihypertensive agents were added before the post-conversion blood pressure measurements were taken. Since the benazepril blood pressure evaluated in this analysis was the first recorded after the medication change, no interim clinic visits would have occurred during which additional agents could have been added. Because this analysis compared only one blood pressure measurement after patients began receiving benazepril, it is impossible to determine if the dosage was adjusted later. However, since the blood pressures before and after the change were the same, it is unlikely that significant dosage change was required.

Any difference in the measured parameters was assumed to be due to the ACE inhibitor, an assumption which may have been invalid. Unlike the previous trial by Lindgren-Furmaga et al.1 in which enalapril and lisinopril were evaluated, we found no change in blood pressure control following the conversion of lisinopril to benazepril. It is possible that are more pharmacologically similar than enalapril and lisinopril. Also, the small sample size of the previous study may have influenced the results compared with our larger patient population.

The population evaluated in this study was not limited to patients receiving an ACE inhibitor exclusively for the treatment of hypertension. The results, therefore, reflect the effects of medication conversion in a general population. Although the therapeutic response cannot be determined for treatment of conditions such as diabetic nephropathy and congestive heart failure in this study, the effects on blood pressure, potassium, and serum creatinine appear to be the same when benazepril is substituted for lisinopril in these patients. Therefore, patients treated for these conditions should not require dosage adjustment or additional monitoring to prevent problems with one of these factors after drug conversion.

At the time of the formulary conversion, costs to the Medical Center for lisinopril 5, 10, and 20 mg tablets were $0.317, $0.275, and $0.37. The cost for all strengths of benazepril tablets (5, 10, 20, and 40 mg) was $0.247. During the nine-month period before the conversion, the cost of treating 1,288 patients with ACE inhibitors was $163,894. In the nine-month period after the conversion, the cost of treating the same number of patients was $127,508. Over this period actual drug cost savings were $36,386, with an extrapolated annual savings of nearly $50,000. This figure represents only the actual drug cost savings.

Our study design, unlike that of McDonough et al., did not determine the incidence of adverse effects for lisinopril and benazepril, or evaluate the frequency of clinic visits and laboratory monitoring. This study does demonstrate that patients who tolerate lisinopril can be converted to benazepril without an increase in serum creatinine and serum potassium levels, which are two of the most serious and common adverse effects associated with ACE inhibitor use.

We were unable to determine if patients made more clinic visits after conversion to benazepril. However, since there were no changes in blood pressure response or elevations in laboratory parameters, increased monitoring should not have been necessary. Even if additional monitoring was performed, it should not have increased costs enough to substantially affect the overall cost savings provided by lower drug acquisition costs, as shown in the McDonough study.

CONCLUSION

There were no clinically significant differences found in blood pressure, serum potassium, or serum creatinine following conversion of lisinopril to an equivalent dosage of benazepril in patients receiving stable doses. Routine additional monitoring of these parameters following conversion does not appear to be necessary. When benazepril was substituted for lisinopril in an equivalent daily dose, the annual drug cost savings at our institution totaled almost $50,000.

References