Effect of Indapamide on Blood Pressure and Glucose Tolerance in Non-Insulin-Dependent Diabetes

Andrew D. B. Harrower, Gary McFarlane, Thomas Donnelly, and Christina E. Gray

SUMMARY Ten hypertensive non-insulin-dependent diabetic patients were treated with the antihypertensive drug indapamide to assess its effect on glucose tolerance over 1 year. Both systolic and diastolic blood pressures fell significantly (p < 0.001) over the first month of treatment, and no change in plasma glucose or plasma insulin levels during an oral glucose tolerance test occurred at any time. Indapamide is an effective antihypertensive drug and, in contrast to thiazide diuretics, has no adverse effect on glucose tolerance in non-insulin-dependent diabetic patients.

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Key Words • plasma glucose • plasma insulin • oral glucose tolerance test

Thiazide diuretics are widely used for the treatment of hypertension. They are generally effective in many patients with mild to moderate disease but can have significant metabolic side effects. The reported deterioration in glucose tolerance during prolonged administration is of some concern, particularly during treatment of non-insulin-dependent diabetes. In such patients, in contrast to those who do not have diabetes, further glucose intolerance develops within a few months of starting thiazide treatment.

Indapamide was introduced as an antihypertensive agent with minimal diuretic activity and significant antihypertensive effects. As several reports have shown no deterioration in glucose tolerance during treatment with indapamide, the drug was assessed in a group of patients with non-insulin-dependent diabetes to determine whether diabetic control deteriorated.

Patients and Methods

Ten non-insulin-dependent diabetic patients aged from 39 to 71 years gave informed consent to the study. Diabetes had been diagnosed initially on the basis of classic symptoms and random plasma glucose levels greater than 15 mmol/L. All had been found to be persistently hypertensive after repeated measurements over 1 month. Hypertension was defined as either systolic pressure greater than 165 mm Hg or diastolic pressure greater than 95 mm Hg or both. Patients with secondary hypertension due to renal disease or endocrine disorders were excluded. No patient had had previous antihypertensive drug treatment. Two were taking chlorpropamide and the other eight controlled their disease with diet alone. All had normal plasma creatinine levels.

An oral glucose tolerance test (OGTT) with a 50-g glucose loading dose was carried out before, after 1 month, and after 1 year of treatment with indapamide, 2.5 mg daily. Blood samples were obtained at 30-minute intervals for 2 hours and analyzed for glucose and insulin concentrations. Blood pressure was measured on each visit with an appropriate-size cuff after the patient had rested supine for at least 10 minutes. Statistical analysis was by Wilcoxon test for paired differences.

Results

Either systolic or diastolic pressure or both fell in all 10 patients (Figure 1) and no patient had side effects during treatment. Mean systolic and diastolic blood pressures fell significantly after 1 month (p < 0.001) with no further significant fall after 1 year (Table 1). No significant changes occurred in glucose tolerance, and the area under the curve during the OGTT remained the same for both glucose and insulin (Table 1). None of the patients required any change in diabetic treatment. No significant change occurred in plasma potassium or plasma creatinine levels. Mean (±sd) body weight was 69.49 ± 11.25 kg before treatment and 69.27 ± 10.21 kg after 1 year (not significant).
FIGURE 1. Systolic and diastolic blood pressures before, after 1 month, and after 1 year of indapamide treatment in 10 patients with non-insulin-dependent diabetes.

Discussion

The mechanism by which glucose tolerance is impaired by thiazide treatment is unclear, but there is considerable evidence that hypokalemia is a factor.\(^3\),\(^5\),\(^12\)-\(^16\) This may be a result of insulinopenia,\(^15\),\(^17\) diminished beta cell responsiveness to the glucose stimulus,\(^18\) or impaired conversion of proinsulin.\(^15\) Impaired glucose tolerance can also be prevented or reversed by administration of potassium.\(^16\)-\(^20\) Indapamide does not appear to have the same effect on serum potassium levels as thiazides,\(^21\),\(^22\) which may explain failure of the drug to affect glucose tolerance adversely. This study confirmed 1) that indapamide is an effective antihypertensive agent and 2) it causes no deterioration in glucose tolerance in non-insulin-dependent diabetic patients during 1 year of treatment. Although there was no preceding placebo phase, there was a run-in period to confirm persistent hypertension and to familiarize the patients with the procedures.

In view of the concern that the long-term effects of thiazide diuretics on glucose tolerance may substitute one cardiovascular risk factor for another,\(^2\) an alternative drug should perhaps be sought. Current evidence suggests that indapamide should be considered as an alternative to thiazide treatment, particularly in hypertensive diabetic patients.

<table>
<thead>
<tr>
<th>Time</th>
<th>Blood pressure (mm Hg)</th>
<th>Area under OGTT curve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>Before treatment</td>
<td>178.5±7</td>
<td>105.5±3</td>
</tr>
<tr>
<td>After 1 month</td>
<td>161.5±7</td>
<td>88.5±2.5</td>
</tr>
<tr>
<td>After 1 year</td>
<td>162±7</td>
<td>85.5±3</td>
</tr>
</tbody>
</table>

Values expressed as means ± SEM. OGTT = oral glucose tolerance test.
References


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