Spironolactone Attenuates Oxidative Stress in Patients With Chronic Kidney Disease

To the Editor:

In one of the latest issues of *Hypertension*, Michea et al\(^1\) reported that the mineralocorticoid receptor antagonist spironolactone attenuates cardiac hypertrophy and oxidative stress of the heart in uremic rats. The results of our recent clinical study indicate that spironolactone acts to decrease the amount of oxidative stress in patients being treated for chronic kidney disease. In an open, randomized, crossover study, 16 white adult patients (10 men and 6 women; mean age: 41 years) with nondiabetic proteumuric chronic kidney disease were evaluated to test the hypothesis that spironolactone combined with standard nephroprotective therapy may act as a clinically beneficial antioxidant.

All of the study participants, during a preliminary period of 8 weeks, received the angiotensin-converting enzyme inhibitor cilazapril (5 mg), angiotensin II type 1 receptor blocker telmisartan (80 mg), and diuretic hydrochlorothiazide (12.5 mg), reducing the blood pressure to <130/80 mm Hg. The trial treatment was either based solely on the unchanged double blockade of the renin-angiotensin system or combined with 25 mg of spironolactone, thus providing triple renin-angiotensin system blockade during the first 2 months of the study, with the alternative being used for the next 2 months. A commercial ELISA kit (Cayman Chemical Co) was then used to measure the urinary excretion of 15-F\(_2\)t-isoprostane, widely accepted as a reliable and sensitive marker of oxidative stress in the human body.\(^2\)

It was found that spironolactone significantly reduced urinary levels of 15-F\(_2\)t-isoprostane relative to the control group (ANOVA \(P=0.035\); posthoc \(P=0.041\)), with no change observed in systemic blood pressure or serum creatinine levels (Table). This finding may be of clinical relevance, because 15-F\(_2\)t-isoprostane isoprostane has biological activity as a potent renal vasoconstrictor\(^3\) and has been implicated as a causative mediator in hepatorenal syndrome.\(^4\)

Interestingly, Furumatsu et al\(^5\) recently observed a beneficial effect from the incorporation of spironolactone into a combined treatment regimen consisting of angiotensin-converting enzyme inhibitor and angiotensin II type 1 receptor blocker for use against chronic kidney disease; Furumatsu et al\(^5\) specifically noted improved intrarenal hemodynamics, as well as decreased proteinuria levels, in patients receiving spironolactone. Thus, taken together with the findings of previous studies, our results indicate that spironolactone may be a useful addition to standard nephroprotective therapy, playing a beneficial role as a clinically effective antioxidant.

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**Disclosures**

None.

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**Table. Serum Creatinine and Urinary Excretion of 15-F\(_2\)t-Isoprostane**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Randomization</th>
<th>Spironolactone</th>
<th>Control</th>
<th>End of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine, mean± SEM, mg/dL</td>
<td>1.12±0.08</td>
<td>1.16±0.10</td>
<td>1.13±0.11</td>
<td>1.09±0.10</td>
</tr>
<tr>
<td>Urinary 15-F(_2)t-isoprostane, geometric mean (95% CI), ng/mg of creatinine</td>
<td>0.76 (0.48 to 2.48)</td>
<td>0.65 (0.51 to 0.98)</td>
<td>0.94 (0.67 to 2.55)</td>
<td>0.91 (0.55 to 2.51)</td>
</tr>
</tbody>
</table>

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