Spironolactone Attenuates Oxidative Stress in Patients With Chronic Kidney Disease

To the Editor:

In one of the latest issues of Hypertension, Michea et al 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 proteinuric 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-F2t-isoprostane, widely accepted as a reliable and sensitive marker of oxidative stress in the human body.

It was found that spironolactone significantly reduced urinary levels of 15-F2t-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-F2t-isoprostane isoprostane has biological activity as a potent renal vasoconstrictor and has been implicated as a causative mediator in hepatorenal syndrome.

Interestingly, Furumatsu et al 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 specifically noted improved intrarenal hemodynamics, as well as decreased proteinuria levels, in patients receiving spironolactone. Thus, 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.

Source of Funding

The study was fully supported by Medical University of Gdansk via ST-U grant.

Disclosures

None.

Marcin Renke
Leszek Tylicki
Department of Nephrology, Transplantology and Internal Medicine
Medical University of Gdansk
Gdansk, Poland

Narcyz Knap
Department of Medical Chemistry
Medical University of Gdansk
Gdansk, Poland

Przemysław Rutkowski
Department of Nephrology, Transplantology and Internal Medicine
Medical University of Gdansk
Gdansk, Poland

Alexander Neuwelt
Blood Brain Barrier and Neuro-Oncology Program
Oregon Health and Science University
Portland, Ore

Wojciech Łarzyński
Department of Nephrology, Transplantology and Internal Medicine
Medical University of Gdansk
Gdansk, Poland

Michał Woźniak
Department of Medical Chemistry
Medical University of Gdansk
Gdansk, Poland

Bolesław Rutkowski
Department of Nephrology, Transplantology and Internal Medicine
Medical University of Gdansk
Gdansk, Poland

Table. Serum Creatinine and Urinary Excretion of 15-F2t-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-F2t-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>


Spironolactone Attenuates Oxidative Stress in Patients With Chronic Kidney Disease
Marcin Renke, Leszek Tylicki, Narcyz Knap, Przemyslaw Rutkowski, Alexander Neuwelt, Wojciech Larczynski, Michal Wozniak and Boleslaw Rutkowski

Hypertension. 2008;52:e132-e133; originally published online September 29, 2008;
doi: 10.1161/HYPERTENSIONAHA.108.120568

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/52/5/e132

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/