Hypertensive Patients That Respond to Aldosterone Antagonists May Have a Nonclassical 11β-HSD2 Deficiency

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To the Editor: Recently, Dudenbostel, and Calhoun[1] showed the benefits of aldosterone antagonists for blood pressure control in resistant hypertension patients with normal or low aldosterone levels, suggesting a mineralocorticoid-dependent mechanism, similar to patients carrying an 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) deficiency. However, another recent publication by the same group (Ghazi and Calhoun)[2] shows that 11β-HSD2 activity evaluated by urinary free cortisol to cortisone ratio is similar in patients with resistant hypertension compared with the control group. Nevertheless, we and others have shown that essential hypertensive patients have an increased cortisol to cortisone ratio both in urine and serum samples when compared to normotensive subjects.[3,4] In addition, we have also reported that low renin essential hypertensive patients have serum F/E ratios, which negatively correlate to serum aldosterone and plasma renin activity.[3]

The background of the population studied and the type of samples analyzed could explain the differences between these results. We carried out our study in a Chilean population, which in terms of ethnicity is predominantly Spanish/White-Amerindian, while the population studied by Calhoun was around 50% African American. On the other hand, there is evidence that determinations of the F/E ratio in order to detect an impairment of 11β-HSD2 activity could be less sensitive in 24-hour urine than in serum samples.[5] This last issue could be explained because cortisol concentrations are higher in the early morning than the rest of the day, providing more substrate for the enzyme to inactivate cortisol to cortisone, while in 24-hour urine samples, the nadir of cortisol's concentration in the afternoon–evening could minimize the changes in the F/E ratio, resulting in false-negative results. Therefore, serum F/E ratio could be a better parameter to detect partial impairment of 11β-HSD2 activity.

We are aware there are different methods for measuring cortisol and cortisone, which could lead to different results, being the most suitable one the high-performance liquid chromatography in combination with tandem mass spectrometry, given the high specificity, accuracy, reproducibility, and analytical sensitivity required for the determination of these steroids.

In summary, we suggest that some hypertensive patients with normal or low aldosterone levels responding to aldosterone antagonists may carry a nonclassical 11β-HSD2 deficiency, supporting the treatment with these kinds of drugs. This deficiency could be secondary to exogenous or endogenous enzyme inhibitors or epigenetic changes in HSD11B2 gene, but further studies are needed.

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DISCLOSURE

The authors declared no conflict of interest.

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