Drug Design, Development and Therapy

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LETTER

Letter regarding the article, "A randomized, double-blind clinical trial of canrenone vs hydrochlorothiazide in addition to angiotensin II receptor blockers in hypertensive type 2 diabetic patients"

This article was published in the following Dove Medical Press journal:
Drug Design, Development and Therapy

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Dear editor

Previous studies have confirmed the utility of canrenone to control inflammation, microalbuminuria, and cardiovascular risk.[1,2] Recently, we read with great interest the study by Derosa et al.[3] The authors performed a randomized, double-blind clinical trial to compare the effectiveness of canrenone vs hydrochlorothiazide (HCTZ) in addition to angiotensin II receptor blockers (ARBs) in patients with hypertension and type 2 diabetes mellitus. The primary endpoints were blood pressure, glycemia, lipid profile, potassium, aldosterone, and renal function. They concluded that the effect on blood pressure was similar between canrenone and HCTZ. Nevertheless, the metabolic parameters were improved in patients taking canrenone; thus, it was worsened in those receiving HCTZ. The research appears informative clinically. Thus, some issues should be addressed in interpreting the results.

First, although canrenone was associated with improved efficiency in some metabolic parameters compared with HCTZ, the statistical difference did not translate into clinical importance. For instance, the mean HbA_{1c} decreased from 7.2% to 7.1% after 1-year follow-up in the canrenone group, while it increased from 7.5% to 7.8% in the HCTZ group. The difference was statistically significant. Nevertheless, the magnitude of HbA_{1c} reduction in the canrenone group was slight, and the final HbA_{1c} level did not meet the control target for particular population according to The American Diabetes Association guideline.[4] Similarly, although canrenone was associated with lower level of low-density lipoprotein-cholesterol (LDL-C) relative to control drug, the final LDL-C level still did not meet the target value. Theoretically, the target value should be <70 mg/dL in patients with diabetes mellitus.[5] Therefore, the statistical significance does not mean the clinical significance.

Second, the use of ARB may be associated with an elevation in serum creatinine level.[6] This effect was different among the different dosage of ARB. However, the individual ARB and the dosage of ARB were not reported in this study. In addition, the LDL-C level was high among the included patients. It is unclear whether these patients received the statin to reduce the lipid concentrations or not. Therefore, the study methods are critical for the study validity.

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http://dx.doi.org/10.2147/DDDT.S185297

Third, the lower estimated glomerular filtration rate (eGFR) was observed in the group with HCTZ, which would be associated with the administration of a very high dose of the diuretic drug (HCTZ).

Fourth, in part of the study group, the dose of canrenone and HCTZ was increased if blood pressure had not been controlled (<140/90 mmHg). Nevertheless, the information on the proportion of patients using the higher dose of canrenone and HCTZ was unclear. Moreover, are there any other hypotensive drugs used beyond treatment with the higher dose of canerone and HCTZ if the blood pressure was not controlled?

Fifth, the information concerning the stage, time, and any complications of hypertension (eg, left ventricle hypertrophy and albuminuria) were also not reported.

Above all, we should be more prudent to evaluate the data to draw a reliable conclusion. Evidence from a more substantial number of participants on the hard endpoint concerning canrenone is warranted in the future.

Disclosure

The authors report no conflicts of interest in this communication.

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