Black Pearl in the LIFE Study: Angiotensin-II Receptor Blockade on Atrial Fibrillation for Future Personalized Medicine

The LIFE study by Wachtell et al. (1) presented evidence indicating that losartan significantly reduces new-onset atrial fibrillation (AF) in comparison to atenolol-based antihypertensive treatment and thereby supports recent studies in this field (2,3). Conversely, the LIFE study revealed that new-onset AF was more frequent in losartan-treated blacks (1.9%) than in atenolol-treated blacks (0.8%). In addition, van der Hooft’s report explained that losartan was one of several drugs that possibly could induce AF (4). Moreover, the occurrence of AF tended to be more frequent in the valsartan group (2.4%) than in the amlodipine group (2.0%) in the VALUE trial (5).

These results surprised and persuaded us to move forward with our own study of AF. We hypothesize that certain types of AF are associated with reduced activation of the renin-angiotensin system (RAS), especially in patients with a small left ventricular cavity (SLVC) due to hypertrophy (6–8). The mechanism of the development of AF in these patients remains unclear. However, we do know that the RAS regulates sodium balance, intravascular volume, and blood pressure. As a result, inhibiting the RAS in patients with an SLVC may induce hypotension, increased heart rate, and hypercontraction due to systolic emptying, which may be related to the autonomic effects on pulmonary venous foci and AF (6–8).

Blacks were reported to have more severe left ventricular (LV) hypertrophy than whites with similar levels of hypertension (9). In addition, multivariable-adjusted LV internal dimensions are smaller in blacks than in whites (9), suggesting that SLVC may be more common in black than white hypertensive patients. Taking these data into consideration, our speculation may be compatible with a part of the LIFE or VALUE study results.

Because of the small percentage (10%) of participants who underwent echocardiographic assessments in the LIFE study (1), the true severity of LV hypertrophy and the LV cavity size are unclear. Commonly used electrocardiographic criteria for detection of LV hypertrophy were reported to have poor sensitivity among both black and white hypertensive patients (10). We suggest that future studies should analyze whether or not the incidence of AF differs in the presence of an SLVC owing to hypertrophy between drug groups.

In conclusion, although an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker may prevent most types of AF, they also may in fact provoke the development of certain types of AF in SLVC patients. Our speculation needs to be confirmed among hypertensive patients with an SLVC due to hypertrophy in a large-scale randomized clinical trial. These analyses may show a more optimal choice for initial pharmacotherapy of hypertension for future personalized medicine.

REFERENCES


REPLY

We would like to thank Dr. Ogimoto and colleagues for their interest in our study showing that losartan reduced the incidence of new-onset atrial fibrillation (AF) by 33% compared to atenolol (1). Dr. Ogimoto and colleagues note that the incidence of new-onset AF is numerically higher among black patients treated with losartan compared to those treated with atenolol. However, the data we presented do not provide statistical support for a difference in the incidence of new-onset strokes between blacks on losartan-based compared to atenolol-based treatment (n = 5 [1.9%] vs. 2 [0.8%]; HR [hazard ratio] = 2.5 [95% confidence interval 0.48–12.8], p = 0.279). Furthermore, there was no association of black versus white ethnicity and new-onset AF (p = 0.11). Thus, the LIFE data do not document ethnic differences in either new-onset AF or treatment effects thereon.