Paramount Importance of Angiotensin ReceptorNeprilysin Inhibitor in Heart Failure Management

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Heart failure (HF) is still one of an enormous health problem worldwide. Many diseases such as coronary artery disease (CAD) and cardiomyopathy progress to HF thus increasing morbidity and mortality rates (1,2). HF is linked with various neurohormonal pathways such as renin-angiotensin-aldosterone-system (RAAS), sympathetic nervous system (SNS), and natriuretic peptide (NP) (3). The latter pathway has just become an emerged research area in HF management as clinical trial has proven that new drug called angiotensinreceptorneprilysin inhibitors (ARNi) LCZ696 showed superiority in reducing morbidity and mortality when compared with theprevious drug is known with class of recommendation I and level of evidence A which is angiotensin-converting enzyme inhibitor (ACE-I) (4).

NP has arolein controlling sodium and fluid homeostasis (5). There are three types of NPs which are atrial NP (ANP), brain NP (BNP), and C-type NP (CNP). ANP and BNP were released as consequences of increased atrial and filling pressure from atria and left ventricle respectively. On the other hand, CNP is located mainly in central nervous system, kidneys, and vascular endothelial cells (5). Collectively, NP has several advantageous mechanisms of actions include natriuresis, diuresis, vasodilatation, suppression of the RAAS and SNS, antihypertrophic, and antifibrotic effect in HF state (6). Despite its benefits, NPs are degraded by neutral endopeptidase enzyme called neprilysin (1) Therefore, adrug that could inhibit neprilysin action perhaps would be a breakthrough in HF therapy.

ARNi LCZ696 is made of combination the neprilysin inhibitor (Ni) sacubitril and the angiotensin receptor blocker (ARB) valsartan (5). This mixture was chosen because Ni monotherapy showed alack of efficacy in hypertension and HF state (7). On the other hand, acombination of Ni and ACE-I called omapatrilat despite its significant effect on hypertension and HF showed increased of angioedema occurrence in compared with ACE-I alone (8,9).

Prospective comparison of ARNi with an ACE-I to Determine Impact on Global Mortality and Morbidity in HF (PARADIGM-HF) trial compared ARNi LCZ696 (400 mg daily) and enalapril (20 mg daily) in HF reduced ejection fractions (HFrEF) patient outcomes (4,10). ARNi could show its superiority to enalapril with reduced risk of cardiovascular death (4). In addition, LCZ696 group significantly had reduced HF hospitalizations due to aggravating HF (10). Other clinical trials also unveiled significant effect of ARNi in HF preserved ejection fractions (HFpEF) and hypertension patient when compared with valsartan (11,12). Regardless of ARNi superiority compared to ACE-I and ARB in HF state, further studies still need to be conducted in compare with other drug groups such as calcium-channel blocker and diuretic, and more importantly to elucidate its effect and benefit for other indications.

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