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Comparative efficacy of renin-angiotensin aldosteron system modulators and angiotensin receptor neprilyzin inhibitor in chronic heart failure with reduced, mid-ranged and preserved ejection fraction

L. Tumasyan, K.G. Adamyan, A.L. Chilingaryan, L.G. Tunyan, V.A. Mkrtchyan, L.G. Budagyan

Institute of Cardiology, Yerevan, Armenia

The aim of study was to compare efficacy of therapy with ramipril (R, 10 mg) + spironolacton (S, 25 mg), valsartatan (V, 320 mg) + S, sacubitril/valsartan (S/V, 97/103 mg), and S/V+S on prognosis, left (LV) and right ventricular (RV) and atrial (LA) and (RA) functional parameters, NT-pro-BNP (pg/ml), transforming growth factor-beta (TGF-β) and hsCRP (ng/ml) levels in patients (pts) with III NYHA FC heart failure in relation to reduced (HFrEF), mid-ranged (HFmEF) or preserved (HFpEF) ejection fraction (EF).

Methods: 122 pts (age 58.4) with HFrEF (EF$<$50), 108 pts (age 59.9) with HFmEF (40$\leq$EF$<$50) and 104 pts (age 63.1) with HFpEF (EF$\geq$50) in sinus rhythm were randomly assigned to groups, receiving R+S (n=32; 28; 27), V+S (n=30; 27; 26) and S/V (n=31; 27; 26) and S/V+S (n=29; 26; 25) in addition to diuretics and beta-blockers.

Results: 1-year mor-tality and hospitalization (%) were, 40.6 and 73.3; 39.3 and 57.1; 33.3 and 55.5 in R+S; 43.3 and 76.7; 40.7 and 59.3; 38.5 and 57.7 in V+S; 32.3 and 58.1; 29.6 and 48.1 and 30.1 and 42.3 in S/V and 31 and 55.2; 30.8 and 42.3 and 32 and 40 in S/V+S receiving groups with HFrEF, HFmEF and HFpEF, respectively.

Survival analysis revealed RR reduction of 1-year mortality at 20.7 and 23.6; 25.4 and 28.4 and hospitalization at 20.7 and 24.3; 24.7 and 29.3 in HFrEF pts, treated by S/V and S/V+S, compared to R+S and V+S, respectively (p$<$0.05). Similarly, 1-year mortality and hospitalization were reduced at 24.7 and 21.6; 27.3 and 24.3 in HFmEF pts. Significant reduction of 1-year hospitalization at 23.8 and 23.7; 27.9 and 30.7 (p$<$0.05), but not mortality was revealed in V/S and V/S+S treatment group with HFpEF. 1-year S/V and S/V+S treatment significantly (at % from baseline, p$<$0.01) decreased levels of TGF-β at 32.3 and 34.5; 31.3 and 33.3, NT-pro-BNP at 40.3 and 42.3; 38.9 and 40.1, e' at 30.6 and 31.5; 30.2 and 30.6, Ar-A at 56.6 and 58.8; 55.1 and 57.2, RAFI at 34.3 and 35.1; 32.9 and 33.6, LAFI at 35.7 and 36.6; 34.9 and 35.2, LV EF at 23.1 and 24.2; 22.1 and 23.4 in pts with HFrEF and HFmEF, and significant changes of hsCRP at 34.6 and 35.2, levels of TGF-β at 30.2 and 31.2, TAPSE at 42.2 and 43.4, e' at 26.2 and 28.2, PA ET at 19.8 and 20.3 in pts with HFpEF, compared to R+S and V+S, respectively.

Conclusions: 1) S/V and S/V+S treatment associated with significant reduction of morbidity and mortality in pts with HFrEF and HFmEF, and hospitalization in HFpEF compared to use of R+S and V+S. 2) Changes of NT-pro-BNP, Ar-A, RAFI and LAFI, e' $\geq$40%, TGF-β $\geq$30% identified pts with cardiovascular risk reduction in HFrEF and HFmEF groups, while changes of TGF-β, hsCRP$\geq$30%; PAET $\geq$30% revealed pts with improvement of morbidity in pts with HFpEF. 3) Prognostic improvement in pts treated by S/V and S/V+S has related to improvement of TGF-β, LV systolic and diastolic functional parameters, LA and RA functional parameters in HFrEF and HFmEF and to TGF-β, hsCRP, LV diastolic and RV functional parameters changes in HFpEF.