Srce i krvni sudovi 2017; 36(S2): 46-47

Commentary

Comparative analysis of ESC 2016 guidelines and ACC/AHA/HFSA 2016 guidelines about the importance of angiotensin receptor neprilysin inhibitor (ARNI) in the treatment of patients with systolic heart failure

Milan Pavlovic[1]

[1]*Clinic for Cardiovascular diseases, Clinical center Nis, Serbia.*

The 2016 contemporary Guidelines of European Society of Cardiology for diagnostics and treatment of acute and chronic heart failure recommends that the treatment of heart failure with reduced systolic function should be started with ACE inhibitors and beta blockers1. It is necessary to titrate the dosage of these medicaments and increase it gradually to the level of those in great randomized clinical studies that proved to be efficient in mortality reduction in patients with systolic heart failure. Guidelines from 2016 are not different in this matter from those given by previous guidelines for heart failure of European Society of Cardiology. If, beside the treatment with optimal dosages of ACE inhibitors (blockers of angiotensin receptors in patients intolerant to ACE inhibitors) and beta-blockers, a patient with a reduced systolic function and ejection fraction of 35% or less still shows symptoms and signs of heart failure, it is necessary to add the antagonist of mineral corticoid receptors.

If a patient still shows symptoms and signs of heart failure even after full ACE inhibitors therapy (blockers of angiotensin receptors in patients intolerant to ACE inhibitors), beta blockers and antagonists of mineral corticoid receptors, it is necessary to consider the next step in the treatment. One of the therapeutic options is replacing ACE inhibitors (blockers of angiotensin receptors in patients who are intolerant to ACE inhibitors) with an inhibitor of angiotensin receptor – neprilysin (ARNI). A new composite medicament consists of blockers of angiotensin receptors valsartan and neprilysin inhibitor sacubitril. If QRS duration of the electrocardiogram is 130 msec or more a resynchronization therapy may be considered. If patients still have a heart rate over SF 70/min even after therapy with beta blockers with optimal dosage (maximum tolerated dosage), the addition of ivabradine to the therapeutic list should be considered.

From the initiation of treatment of patients with heart failure diuretics are used optionally, as a symptomatic treatment for congestion. It is important to consider the indication for ICD implantation in a primary or secondary prevention of sudden cardiac death.

The 2016 contemporary Guidelines of European Society of Cardiology suggest replacement of ACE inhibitors (blockers of angiotensin receptors in patients intolerant to ACE inhibitors) with an inhibitor angiotensin receptor–neprilysin (ARNI) as a possible therapeutic procedure. The objective is to increase efficiency in the treatment of patients with systolic heart failure and the improvement of patient`s prognosis. ACE inhibitors reduce the mortality of patients with systolic heart failure by 18%, blockers of angiotensin receptors showed to be slightly less effective in the reduction of mortality by 15%. Beta blockers presented better results in the reduction of mortality by 34%, antagonists of mineral corticoid receptors 25% and ICD implementation 26%.

2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure raised ARNI inhibitor to a higher level in the therapeutic algorithm and suggested it as a starting option in the treatment of patients as an alternative therapy for ACE inhibitors (a blocker of angiotensin receptors in patients intolerant to ACE inhibitors)[2,3]. The contemporary American guidelines suggest ARNI inhibitors as a starting option in the treatment of patients with heart failure and reduced ejection fraction below 40% (class I level of evidence B), together with beta blockers and antagonists of mineral corticoid receptors. ARNI inhibitor reduces the mortality of patients with systolic heart failure by 38%. The conceptual principle of the conventional therapy by ACE inhibitors (blockers of angiotensin receptors in patients intolerant to ACE inhibitors) beta blockers and antagonists of mineral corticoid receptors was the blockage of excessive neurohumoral activation in chronic heart failure. Apart from this conceptual principle ARNI inhibitor (blockers angiotensin receptor valsartan) includes stimulation and intensifying of adaptive mechanisms in heart failure through increasing the concentration of endogen vasoactive peptides (neprilysin inhibitor sacubitril). The levels of natriuretic peptides and bradykinin are increased by the blockage of neprilysin receptors. In this way, the adaptive mechanisms of heart failure are stimulated with the final result in vasodilatation, the reduction of progression in myocardium fibrosis, the reduction of salt retention and the reduction of excessive neurohumoral activation as well.

Address for correspondence: Pavlovic Milan, Klinika za kardovaskularne bolesti, Klinicki centar Nis, Srbija, Email: milanpa@eunet.rs

Composite drug ARNI inhibitor contains the blockers of angiotensin receptors valsartan and the inhibitor of neprilysin receptor sacubitril. This composite medicament was tested in PARADIGM-HF study, in III clinical phase, on over 8000 patients[4]. Patients were randomized on ARNI inhibitor with the dosage of 200 mg twice a day and on enalapril of 10 mg twice a day. ARNI inhibitor showed improvement in patient`s prognosis and the reduction of cardiovascular mortality by 20% compared to enalapril, in recommended dosage by the guidelines for the treatment of heart failure. The overall mortality in patients was reduced by 18 % by using ARNI inhibitor.

European recommendations differ from those of American guidelines regarding introduction of ARNI inhibitor in later phases of the therapeutic algorithm, after previous standard ACE inhibitor therapy (blockers of angiotensin receptors in patients intolerant to ACE inhibitors), beta blockers and antagonists of mineral corticoid receptors. The reason for a more reserved approach in the 2016 Guidelines of European Society of Cardiology for diagnostics and treatment of acute and chronic heart failure is a need for accumulation of experience from a more extensive clinical practice especially regarded side effects. ARNI inhibitor showed in PARADIGM-HF trial a slightly higher incidence of angioedema, without statistical significance. The suggestion of European guidelines is to check the usage of the new drug before it is recommended widely and the treatment of patients with systolic heart failure. The intention of European recommendations is also to check the efficacy of ARNI inhibitor in the group of patients with a less impaired left ventricle systolic function. Although ARNI inhibitor has not revealed any adverse clinical effects on cognitive functions, it has been noticed that in some patients an increase of beta-amyloid peptide can occur in cerebrospinal liquor. The suggestion of European guidelines is to check additionally in practice the effects of the new drug on cognitive functions before its wider usage as a drug for the initiation of systolic heart failure treatment.

References

1. Ponikowski P, Voors A, Anker S, Bueno H, Cleland J, Coats A : 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). European Heart Journal 2016; doi:10.1093/eurheartj/ehw128.
2. Yancy C, Jessup M, Bozkurt B, Butler J, Casey D, Colvin M, et al : 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol 2016; 68:1476–1488.
3. Yancy C, Jessup M, Bozkurt B, Butler J, Casey D, Colvin M, et al : 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure ACCF/AHA Task Force on Practice Guidelines. Circulation 2016;doi: 10.1161/CIR.0000000000000435.
4. McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014; 371:993-1004.