Folia Cardiologica 2019
vol. 14, no. 4, pages 420–421

ISSN 2353–7752

Empagliflozin in heart failure — new facts

Commentary on the article: Cessation of empagliflozin treatment in a hospitalised patient with exacerbated heart failure and reduced ejection fraction. Folia Cardiol. 2019; 14(2): 199–205

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Artykuł jest tłumaczeniem komentarza: Lelonek M. Empagliflozyna w niewydolności serca — nowe fakty. Komentarz do artykułu: Przerwa w terapii empagliflozyną u pacjenta z niewydolnością serca z obniżoną frakcją wyrzutową i hospitalizacja z powodu zaostrzenia niewydolności serca. Folia Cardiol. 2019; 14(2): 199–205. Folia Cardiol. 2019; 14 (4): 418–419. DOI: 10.5603/FC.2019.0096. Należy cytować wersję pierwotną

The article by Komorowska et al. presented the current state of knowledge regarding the effect of empagliflozin on the cardiovascular system based on the description of a clinical case of heart failure with reduced ejection fraction (HFrEF) and concomitant diabetes [1]. The patient in question was burdened with numerous cardiovascular risk factors and comorbidities. The patient obtained 26 points in the MAGGIC (Meta-Analysis Global Group in Chronic Heart Failure) scale, which translates into a high annual mortality of 17.5% and a high three-year death rate of 39.7%.

Currently, the patient remains under observation which has been maintained for 15 months since the re-onset of empagliflozin therapy. During this time, there has been no hospitalisation for exacerbation of heart failure (HF) or for any other reason, there were no outpatient visits requiring an increase doses in diuretics, and there was no need to modify the therapy used. It is worth stating that the patient has been optimally treated for HFrEF since the last hospitalisation in May 2018, including with the drug sacubitril/valsartan at a target dose of 97/103 mg *bis die* (BD).

Empagliflozin is well tolerated in this patient. There have been no incidents of hypoglycaemia or ketoacidosis. No gastrointestinal complaints or fungal infections have been recorded, and kidney function has not deteriorated.

Empagliflozin is one of a new group of sodium and glucose co-transporter type 2 (SGLT2) inhibitor drugs dedicated to diabetes therapy. The drug came to the attention of cardiologists after the publication of the results of the EMPAREG-OUTCOME study [2, 3]. Empagliflozin is today the most selective and best-understood SGLT2 inhibitor.

It is known from the EMPAREG-OUTCOME study that, in diabetic patients, empagliflozin improves the prognosis compared to a placebo in reducing the risk of total mortality, cardiovascular mortality, three-point MACE (major adverse complicating events *i.e.* non-fatal myocardial infarction, non-fatal stroke and cardiovascular death) and the risk of HF hospitalisation [3], regardless of the initial load of myocardial infarction, stroke and cardiovascular risk calculated according to the TIMI (Thrombolysis in Myocardial Infarction) Risk Score for secondary prevention [4] and regardless of glycaemic status [5]. Both high- and low-risk patients have an improved prognosis.

The clinical benefit of empagliflozin therapy has also been documented in terms of greater life expectancy for all age groups [6]. However, patients aged 45 and under, for whom the survival improvement has been calculated to be 4.5 years, benefit the most. According to the data produced by the EMPAREG-OUTCOME study, the patient in question has a chance of prolonging life by 3.1 years [6].

Real-world evidence (RWE) data from the EMPRISE (Empagliflozin Comparative Effectiveness and Safety) study including 35,000 patients has supplemented the results of EMPAREG-OUTCOME, and confirmed the efficacy and safety of empagliflozin therapy compared to the dipeptidyl peptidase 4 (DPP-4) inhibitor — sitagliptin, which is an optimal comparator due to the similar profile of hypoglycaemic

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effect and neutral effect on cardiovascular endpoints [7]. The use of empagliflozin at both doses was associated with a reduced risk of HF hospitalisation in routine clinical practice compared to sitagliptin [hazard ratio (HR) 0.56, 95% confidence interval (CI) 0.43–0.73, p < 0.0001). The effect of empagliflozin on reducing the risk of hospitalisation due to HF was similar in patients with and patients without confirmed cardiovascular disease.

The results of studies conducted so far have allowed the inclusion of SGLT2 inhibitors in the 2016 recommendations of the European Society of Cardiology (ESC) for HF [2], the 2018 recommendations of the American College of Cardiology (ACC) for risk reduction in patients with diabetes and cardiovascular diseases [8], the 2019 expert position of the ESC Heart Failure Association [9], and the 2019 ACC/AHA guidelines for primary prevention of cardiovascular diseases [10].

Further studies dedicated to patients with HF, both with and without diabetes, will determine the significance and role of empagliflozin and other SGLT2 inhibitors in the therapy of patients with HF.

Conflict(s) of interest

The authors are participating in a clinical trial using empagliflozin.

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