Sodium-glucose cotransporter type 2 inhibitors: A new era in the pharmacological treatment of heart failure with reduced ejection fraction?

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Abstract

In the past decades a wide number of drugs have been approved for the treatment of heart failure. Sacubitril/valsartan and ivabradine have been the most recent drugs included for the management of heart failure with reduced ejection fraction. Nowadays, sodium glucose cotransporter type 2 inhibitors have emerged as a feasible choice for the treatment of type 2 diabetic patients with heart failure. These drugs have demonstrated to reduce the risk of hospitalization in patients with heart failure and recent data suggest that these outcomes can be also seen in non-diabetic patients. These promising outcomes will open the possibility that these drugs could be approved for the treatment of heart failure in diabetic patients and a new era in the management of this condition is advised.

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70 beats per minute. Both sacubitril/valsartan and ivabradine have been the most recent approved drugs for HFrEF treatment. However, investigations to find new drugs to treat these patients are ongoing with promising results.

Sodium-glucose cotransporter type 2 inhibitors, the most recent approved hypoglycemic drugs have been associated with a reduced risk of HF hospitalization. Three large randomized controlled trial (EMPA-REG-OUTCOMES [13], CANVAS [14] and DECLARE TIMI 58 [15]) evaluated the safety and benefits of empagliflozin, canagliflozin and dapagliflozin respectively in type 2 diabetic patients with high cardiovascular risk. As a second end point, these drugs were associated with a reduced risk of HF hospitalizations. No significant differences in side effects were seen in patients taking sodium-glucose cotransporter type 2 inhibitors compared to placebo. The most recent study on these drugs was DAPA-HF [16]. This study evaluated the use of dapagliflozin in 4744 patients with HFrEF (left ventricular ejection fraction of 40% or less), New York Heart Association II-IV to receive dapagliflozin or placebo. All patients were receiving guide-based recommended therapy. After a median follow-up of 18.2 months, the composite end point of worsening HF or cardiovascular death was significantly reduced in the dapagliflozin group (HR: 0.74; 95% IC: 0.65-0.85; p<0.001). These findings were similar in patients with and without diabetes mellitus.

Results of DAPA-HF have generated a great debate in the medical community about the benefits of sodium-glucose cotransporter type 2 inhibitors in patients with HF. This group of drugs, beyond hypoglycemic effects also have diuretic, natriuretic, antihypertensive, anti-inflammatory and antiremodelling effects which could explain in part, the positive outcomes in HF patients [17]. Additionally, sodium-glucose cotransporter type 2 inhibitors have been demonstrated to reduce the risk of kidney failure and cardiovascular events in type 2 diabetic patients with kidney disease [18] and improve left ventricular diastolic functional parameters in type 2 diabetic patients and HF [19].

After these results, sodium-glucose cotransporter type 2 inhibitors may represent the first line for treating patients with type 2 diabetes mellitus and HFrEF. However, if these drugs will constitute also a recommendation in HFrEF patients without diabetes needs further investigation. At this time, the main concern for the use of sodium-glucose cotransporter type 2 inhibitors in non-diabetic patients is the risk of hypoglycemia.

Although the definitive inclusion of sodium-glucose cotransporter type 2 inhibitors as an alternative for treating HFrEF patients’ needs more investigation, the positive results of EMPA-REG OUTCOME, CANVAS, TIMI 58 and the most recent DAPA-HF could represent a new era in the treatment of HFrEF patients.

In conclusion, HFrEF has a complex pathophysiology and the use of several drugs with different mechanisms of action and working in multiple pathways is necessary. The medical community is looking forward to a new era in the development of HFrEF treatments. These new alternatives and others under investigation will likely result in higher survival and better quality of life of our patients.

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