

The new therapeutics for patients with hypertension and diabetes – what can we expect?

Peter M. Nilsson¹

¹ Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Sweden

Received: May 2, 2022, Accepted: May 31, 2022

Over the last few years, we have seen new and important anti-glycaemic drugs being introduced for the treatment of type 2 diabetes, more specifically the SGLT-2 inhibitors and the GLP-1 receptor agonists/analogues (RA). As these new drugs have already proven themselves effective for cardiovascular and renal protection [1], there is a case also to consider them from another perspective – the blood pressure-lowering properties of these drugs. As more than 80% of all patients with type 2 diabetes are known to have established hypertension, it is of great importance that such newer anti-diabetes drugs can also reduce blood pressure (BP) as part of their protective profile. In fact, several recent meta-analyses have concluded that both drugs may lower BP effectively, with a somewhat more pronounced effect associated with SGLT-2 inhibitor treatment [2–4].

For the SGLT-2 inhibitors, it has been shown that both office BP and ambulatory BP can be lowered by a few mmHg in studies *versus* placebo. This may be due to the diuretic effects linked to the natriuresis of these drugs when also glucosuria is promoted. Another mechanism may be found in the modest weight loss induced by SGLT-2 inhibitors or other less well-characterized mechanisms on the arterial wall or endothelial function. A recent meta-analysis from 2019 showed that SGLT-2 inhibitors provoke an average reduction of systolic/diastolic BP of 3.62/1.70 mmHg in 24-h ambulatory

BP. This BP-lowering effect remains unmodified regardless of the dose of SGLT-2 inhibitor and is comparable with the BP-lowering efficacy of low-dose hydrochlorothiazide [2].

Correspondingly, the GLP-1 RA drugs have also shown some BP-lowering effects, according to the office and ambulatory measurements. The mechanism behind this is not fully understood, but most likely, this depends on a relatively pronounced weight loss, at least with some preparations of GLP-1 RA drugs that parallels the reduction of BP. Of particular importance is the vasodilation caused by this drug, most likely from interaction with the endothelium or other structures of the arterial wall. An indirect sign of this vasodilation is the modest increase in heart rate in association with BP lowering [5]. This resembles the effect of insulin (vasodilation) on the vasculature. We also know that GLP-1 RA drugs promote the beta-cell secretion of insulin.

Taken together, these promising properties of the newer anti-glycaemic drugs used to treat patients with the combination of type 2 diabetes and hypertension mean that such drugs should be more widely used by clinicians of different specializations dealing with patients with type 2 diabetes. There might exist a specific indication for the drugs, for example, the protective effects on heart failure and nephropathy of SGLT-2 inhibitors and the protection of atherosclerotic events of GLP-1 RA drugs. Of course, many of these preventive effects are similar to both drugs, for example, the impact on major adverse cardiac effects (MACE). On the negative side, the tolerance of the drugs and adverse effects could be discussed. Even if SGLT-2 inhibitors are generally well-tolerated, some patients might experience urinary tract infections, dermatitis, or even

* Correspondence to: Peter M. NILSSON, MD, PhD, Professor, Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Sweden.
E-mail: peter.nilsson@med.lu.se

more serious (but rare) complications like normoglycaemic diabetic ketoacidosis. For the GLP-1 RA drugs, initial nausea and vomiting might preclude some patients from continuing this therapy.

In summary, introducing these newer anti-diabetes drugs could benefit many patients with type 2 diabetes and hypertension, a prevalent co-morbid risk factor increasing the cardiovascular risk if not controlled and that is often difficult to treat. As resistant hypertension is often encountered as a therapeutic problem in many of these patients, the choice of newer anti-diabetes drugs with BP-lowering properties could improve the clinical control of BP and thereby reduce the cardiovascular risk in general.

Conflict of Interest

The author confirms that there are no conflicts of interest.

References

1. Kawai Y, Uneda K, Yamada T, Kinguchi S, Kobayashi K, Azushima K, Kanaoka T, Toya Y, Wakui H, Tamura K. Comparison of effects of SGLT-2 inhibitors and GLP-1 receptor agonists on cardiovascular and renal outcomes in type 2 diabetes mellitus patients with/without albuminuria: A systematic review and network meta-analysis. *Diabetes Res Clin Pract.* 2022; 183:109146.
2. Georgianos PI, Agarwal R. Ambulatory Blood Pressure Reduction with SGLT-2 Inhibitors: Dose-Response Meta-analysis and Comparative Evaluation with Low-Dose Hydrochlorothiazide. *Diabetes Care.* 2019; 42(4):693-700.
3. Liakos CI, Papadopoulos DP, Sanidas EA, Markou MI, Hatzigelaki EE, Grassos CA, Velliou ML, Barbetseas JD. Blood Pressure-Lowering Effect of Newer Antihyperglycemic Agents (SGLT-2 Inhibitors, GLP-1 Receptor Agonists, and DPP-4 Inhibitors). *Am J Cardiovasc Drugs.* 2021; 21(2):123-137.
4. Tsapas A, Karagiannis T, Kakotrichi P, Avgerinos I, Mantsiou C, Tousinas G, Manolopoulos A, Liakos A, Malandris K, Matthews DR, Bekiari E. Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: A systematic review and network meta-analysis. *Diabetes Obes Metab.* 2021; 23(9):2116-2124.
5. Sun F, Wu S, Guo S, Yu K, Yang Z, Li L, Zhang Y, Quan X, Ji L, Zhan S. Impact of GLP-1 receptor agonists on blood pressure, heart rate and hypertension among patients with type 2 diabetes: A systematic review and network meta-analysis. *Diabetes Res Clin Pract.* 2015; 110(1):26-37.