

Glucagon-Like Peptide 1 Receptor Agonists (GLP1RA) and Sodium-glucose co-transporter-2 inhibitors (SGLT2i): Making a pragmatic choice in diabetes management

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Abstract

The availability of newer glucose-lowering drugs has created opportunities for comprehensive diabetes care. Two classes of drugs, GLP1RA (glucagon-like peptide 1 receptor agonists), and SGLT2i (sodium glucose cotransporter 2 inhibitors) have demonstrated their efficacy in glucose control as well as cardiovascular risk reduction. While both can be used together, there is an ongoing debate regarding their relative advantages and limitations. We present a clinical perspective to compare and control these two classes of drugs, and promote rational prescription in diabetes praxis.

Keywords: Canagliflozin, CV risk reduction, dapagliflozin, dulaglutide, empagliflozin, GLP1RA, liraglutide, obesity, semaglutide, SGLT2i.

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Introduction

Contemporary diabetes management guidelines support the use of glucagon-like peptide1 receptor agonists (GLP1RA) and sodium-glucose co-transporter-2 inhibitors (SGLT2i) as front-line agents.¹ This is because of the robust evidence related to their glucose lowering efficacy as well as cardiovascular safety and benefits.

Both classes of drugs have different mechanisms of action, pleiotropic benefits and side effect profiles. Recommendations do offer guidance as to which drug class to prefer in patients at risk of heart failure, but do not replace clinical judgment. This brief communication assists physicians in choosing between the two types of drugs. It uses a simple 3x3 table to aid in clinical decision making (Table). It must be noted that both GLP1RA and SGLT2i can be co-administered as well.

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Table: GLP1RA vs SGLT2i.

Parameter	Comments
Anticipated advantages	
Route of administration	GLP1RA are available as daily subcutaneous, weekly subcutaneous and oral formulation; SGLT2i are oral
Speed of achieving CV benefit	Slower with GLP1RA; faster with empagliflozin
Appetite	GLP1RA reduce appetite; SGLT2i have no impact
Baseline vasculo-metabolic status	
Baro-phenotype: weight, lipids	GLP1RA reduce weight and improve lipids to a greater extent
Cardio-phenotype: ASCVD, heart failure	GLP1RA modify atherosclerosis; SGLT2i have better results in heart failure
Reno-phenotype	Liraglutide can be prescribed until an eGFR of 15ml/min; SGLT2i are indicated up to an eGFR of 30-45 ml/min
Comprehensive health status	
Comorbid condition	Avoid GLP1RA in diabetic gastroparesis; avoid SGLT2i in active genito urinary infection. Be mindful of contraindications to prescription
Complications	Be watchful for gastrointestinal side effects with GLP1RA; genital infections and ketosis with SGLT2i
Concomitant therapy	Do not co-prescribe GLP1RA with DPP4i; do not use SGLT2i with high dose diuretics or nephrotoxic drugs

Pragmatic Choice

Treatment should be matched to the patient's characteristics, needs and wishes; not the other way round. A detailed clinical assessment is essential to understand the expected benefits and possible risks of GLP1RA and/or SGLT2i therapy in an individual patient.

Both drug classes have some common contraindications: type 1 diabetes, childhood/adolescence, pregnancy and lactation. Beyond this, various molecules are contraindicated in specific situations (liraglutide: medullary thyroid carcinoma, multiple endocrine neoplasia 2; SGLT2i: end stage renal disease, active genitourinary infection).^{2,3}

Both GLP1RA and SGLT2i are preferentially indicated in persons with type 2 diabetes and cardiometabolic risk

factors.⁴ The route of administration, need for reduction in appetite, and expected speed of cardiovascular benefit may influence patient preference for one drug over another (Table). Baseline vasculo-metabolic status, including adiposity, lipid profile, risk of heart failure, status of ASCVD and renal function, also modify choice of therapy. Apart from the vasculo-metabolic health, comprehensive medical status influences clinical decision making. Knowledge of potential risk and side effects of a drug, coupled with information about the patient's health profile, allows for rational prescription.^{5,6}

Summary

Diabetes therapy is a complex and challenging area of medicine. Newer drugs have expanded choices for patients and for prescribers. These include GLP1RA and SGLT2i, both of which are recommended for use in type 2 diabetes. However, it sometimes becomes difficult to decide which drug class to prefer. We have highlighted

simple clinical parameters which assist in this decision making.

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