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CONTINUING EDUCATION

Consultant Pharmacist Continuing Education Series

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Diabetes medications in older persons

Management of type 2 diabetes in older persons should aim to achieve a good quality of life and avoid diabetes-related complications as well as treatment side effects, mainly hypoglycaemia.

Medications for the treatment of type 2 diabetes in older persons include:

- Metformin
- sulfonylureas
- DPP-4 inhibitors
- Acarbose
- GLP-1 RAs
- Thiazolidinediones
- SGLT2 inhibitors
- Insulin

Metformin

Metformin is recommended as first-line therapy for the management of type 2 diabetes in older persons. Metformin has a low hypoglycaemic risk and may cause weight loss and gastrointestinal upset.

The dose should be reduced when renal function in less 90mL/min. Although generally not recommended when creatinine clearance (CrCl) <30 mL/minute, metformin may be considered for patients with stable renal function and CrCl >15 mL/minute, with careful monitoring.

Sulfonylureas

Sulfonylureas include:

- Glibenclamide
- Gliclazide
- Glimepiride
- Glipizide

Sulfonylureas increase pancreatic insulin secretion and may decrease insulin resistance. They have a high risk of hypoglycaemia and are increasingly prescribed less due to this risk and their association with weight gain. Long-acting sulfonylureas (glimepiride, glibenclamide and slow-release gliclazide) have a higher risk of hypoglycaemia.

Dosage reduction may be required in severe impairment because of increased risk of hypoglycaemia; glipizide or gliclazide preferred. Glibenclamide and gliclazide significantly reduce the incidence of diabetes-related microvascular complications; however, they have no cardiovascular benefits. Glibenclamide is associated with an increased risk of cardiovascular mortality compared to gliclazide.

Acarbose

Acarbose improves postprandial hyperglycaemia and has a low hypoglycaemia risk. However, acarbose has a limited role because of gastrointestinal side effects and inferior glycaemic effect compared with metformin and sulfonylureas.

DPP-4 inhibitors

Dipeptidyl peptidase 4 (DPP 4) inhibitors include:

- Alogliptin
- Linagliptin
- Saxagliptin
- Vildagliptin

DPP 4 inhibitors increase glucose-dependent insulin secretion and reduce glucagon production. DPP-4 inhibitors have few adverse effects and a minimal risk of hypoglycaemia, mainly when used with insulin or a sulfonylurea. They do not affect weight.

Renal impairment reduces the excretion of alogliptin, sitagliptin and saxagliptin and dose reduction is required. Linagliptin does not need dose reduction in renal impairment as it is mostly excreted unchanged in the bile.

DPP 4 inhibitors do not increase the risk of major adverse cardiac events, but do not show any cardiovascular or renal benefits. There is an increased risk of hospitalisation for heart failure with saxagliptin and alogliptin.

DPP 4 inhibitors are not usually combined with GLP 1 analogues, as they have similar modes of action, and their combination is unlikely to provide additional clinical benefit.

SGLT2 inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors reduce glucose reabsorption in the kidney and increase its excretion in the urine. They have a low risk of hypoglycaemia. SGLT-2 inhibitors include:

- Dapagliflozin
- Empagliflozin

SGLT-2 inhibitors have significant cardiovascular and renal benefits independent of their glucose-lowering effects. SGLT2 inhibitors reduce plasma glucose, reduce HbA1c, have a diuretic effect, reduce body weight, reduce systolic and diastolic blood pressure, reduce plasma urate and reduce triglyceride levels.

Glucose-lowering efficacy diminishes with declining renal function; however, the cardiorenal benefits are still evident with poor renal function and independent of glucose lowering.

SGLT2 inhibitors significantly reduce the risk of hospitalisation for heart failure and cardiovascular death. The American Diabetes Association guidelines recommend the use of an SGLT2 inhibitors in patients with an eGFR ≥25 mL/min/1.73 m2 and UACR ≥300 mg/g (33.9mg/mmol) to reduce CKD progression and cardiovascular events.

They have an increased risk for genitourinary infections and dehydration, which can contribute to delirium among older persons. SGLT-2 inhibitors also may be problematic in people with urinary incontinence and those who require assistance getting to the toilet.

GLP-1 RAs

Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) include dulaglutide, liraglutide and semaglutide. They increase glucose-dependent insulin secretion and suppress inappropriate glucagon secretion. They also delay gastric emptying, which slows glucose absorption, and decrease appetite.

GLP-1 RAs have multifactorial benefits, reducing glucagon secretion and hepatic glucose production, reducing HbA1c, reducing lipid levels, increasing insulin sensitivity, reducing gastric emptying, promoting natriuresis, as well as promoting weight loss, reducing food intake and increasing satiety. Semaglutide has shown significant benefits in preventing major kidney disease, cardiovascular events, as well as mortality in patients with chronic kidney disease and type 2 diabetes in the landmark FLOW trial.

GLP-1 RAs have low hypoglycaemia risk; however, treatment with insulin or sulfonylureas increases the risk of hypoglycaemia. Gastrointestinal effects are more common in older people. Nausea and/or vomiting occurs in up to 50% of patients; but usually improves with continued treatment.

Insulin

Many older people may still progress to require insulin. Insulin has significant hypoglycaemic risk and increases weight. Basal insulin may have a lower hypoglycaemia risk than premixed insulin in some cases.

Sulfonylureas are often reduced or stopped once insulin therapy is established. Other antidiabetic drugs, eg metformin, may be continued but the insulin dose may need further adjustment.

Use of a pen device is preferred in residential aged care facilities.

Other risks and benefits

The cardiorenal benefits of SGLT2 inhibitors and GLP-1 RAs have been demonstrated in older people aged 65 years and older. Therefore, recommendations for the selection of medications to improve cardiovascular and kidney outcomes do not differ for older people.

As GLP-1 RAs and SGLT2 inhibitors promote weight loss, including lean muscle mass, careful consideration and monitoring is required in frail older patients and those at risk of malnutrition.

Deprescribing should be considered in older people towards end-of-life or limited life expectancy. People with a life expectancy less than 10 years due to age or significant comorbidities are unlikely to gain meaningful benefit from intensive glycaemic control. Residents who have or are at high risk of hypoglycaemia should have the intensity of treatment reduced.

Summary

In older people with type 2 diabetes, treatment should be individualised, with the aim of minimising the incidence of hypoglycaemia while also preventing symptomatic hyperglycaemia. Medications that are more likely to cause hypoglycaemia are best avoided in older patients and greater care is required when using renally cleared medications.

References

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