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The latest updates of diabetes medications

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Glucose control in diabetes deteriorates over time with the progressive nature of disease resulting in risk of developing various micro and macro vascular complications. Many classes of anti-diabetic drugs are available for treatment including metformin, sulfonylureas, glitazones, glinides, α glucosidase inhibitors and nearly a century old insulin. Newer drugs like gliptins (DPP-4 inhibitors), GLP1 agonist, flozins (SGLT-2 inhibitors) and insulin analogs have been added to the list during the last few years. These drugs effectively address various pathophysiological defects. However, given the need for multiple drug therapy, there is still a significant unmet need in the management of T2D. Non-insulin antidiabetic agents have a potential to reduce HbA1c by an average of 1% and the simultaneous use of combination therapy can result in greater HbA1c reduction. Position statement on Standard of Care by ADA, recommends metformin as preferred initial pharmacological agent. These recommendations continue as follows:

• If monotherapy at maximum tolerated dose does not achieve or maintain the target HbA1c, add a second oral or injectable agent.
• Choice of the second agent should be a based on patient-centered approach and should include considerations like efficacy, safety, weight gain, hypoglycaemia risk, cost and patient preference.

Apart from this AACE suggests to start with dual drug therapy if HbA1c is 7.5 or more. If HbA1c is 9 or more at beginning, triple therapy is recommended to start with. If patient is symptomatic at 9 or more HbA1c, insulin should be a part of triple therapy.

DPP4 inhibitors a class of the orally active drugs that enhance incretin system activity by blocking GLP1 degradation. GLP1 is a major incretin hormone responsible for glucose dependent increase in insulin secretion after meals, but its duration of action is shortened by DPP4 enzyme. Increased activity of DPP4 has been seen in diabetic patients resulting in early degradation of incretin. They reduce HbA1C by 0.75%. Benefits over older drugs include very low risk of hypoglycemia, weight neutrality, oral administration and most importantly improving beta cell health. Once-weekly option is also available with potential to improve adherence and effectiveness in long run. Trelagliptin has been well tolerated and produced significant dose-dependent HbA1c reductions in Japanese patients.

Glucagon-like peptide (GLP)-1 agonists are among the most potent drugs for the treatment of T2D. GLP1 agonists increase insulin secretion in response to oral glucose ingestion, induce satiety by slowing gastric emptying, suppresses appetite, inhibit glucagon secretion and also have been proposed to cause ß cell regeneration. Endogenous GLP1 released from intestinal L cells has a short half-life of 4 - 11 min. To overcome this, GLP1 analogs resistant to degradation by DPP4 have been devised.

Sodium glucose co-transporters (SGLT) are located in the proximal tubules of the kidney and are responsible for renal glucose reabsorption from proximal tubules. SGLT2 accounts for 90% of this reabsorption. Up-regulation of renal SGLT2 transporters results in increased reabsorption of glucose from urine and thereby contributing to the total glucose load of the body. SGLT2 inhibitors act on the non-classical pathway and reduce hyperglycaemia by inhibiting renal reabsorption of glucose and thereby increasing urinary glucose excretion. Along with glycemic control these drugs are weight negative (due to calorie loss in urine), mild reduction in blood pressure due to chronic osmotic dieresis and associated with lower risk of hypoglycemia.Insulin remains the most effective blood glucose lowering agent. New basal insulin analogs as well as short acting and ultra short acting analogs that lead to less glucose variability and less hypoglycemia risk with appropriate glycemic targets to achieve in basal and two hours after meal. Newer drugs for management of T2DM seem more comprehensive and protective than earlier ones.