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| Chapter title | Subchapter | Lesson | Content |
| Pharmacological management of diabetes | Treating diabetes to achieve glycaemic goals | Most people with type 2 diabetes require pharmacological treatment to optimize glycaemic management | * Type 2 diabetes is a progressive, chronic disease, which requires lifelong treatment and support. It often requires therapy intensification over time to maintain control of blood glucose. * While lifestyle interventions are the foundation of diabetes management, they are often not sufficient to control blood glucose over the long term, and pharmacological intervention is often required. * In most patients with type 2 diabetes, blood glucose can be adequately managed with medicines included in the WHO Model List of Essential Medicines.      * All people with type 1 diabetes need lifelong treatment with insulin. |
| Prompt initiation and intensification of therapy are essential to improve outcomes for people with type 2 diabetes | * For people with type 2 diabetes, early intervention and timely treatment intensification are important to reduce an individual’s risk of developing complications. * In some circumstances, initial treatment can be lifestyle interventions. However, medications are often needed as the disease progresses. The recommended first-line medication is metformin, followed by the addition of sulfonylureas and then insulin, as needed. * Individuals with diabetes should be reviewed regularly and medications added if not achieving their glycaemic goal. In this video, we will cover when and how to initiate, change or add new therapies in the treatment of type 2 diabetes. * Watch Dr Roopa Mehta discuss oral therapies for type 2 diabetes management.   **<<INSERT VIDEO HERE>>**  Reflection question: How long after recommending lifestyle changes do you usually wait before initiating pharmacotherapy for people with newly diagnosed type 2 diabetes? |
| People with diabetes should have personalized glycaemic targets | * Regular blood glucose testing is important to assess the efficacy of an individual’s diabetes management plan. * HbA1c is the test of choice for monitoring glycaemic control in people with diabetes, where possible, and should be measured at least twice a year. If HbA1c is not available, fasting or post-meal blood glucose is acceptable. * For most people, an HbA1c target of <7% is appropriate, but targets should be adjusted based on personal factors such as age, risk of hypoglycaemia or presence of diabetes complications. * As patients treated with metformin plus lifestyle interventions have a very low risk of hypoglycaemia, a target of <6.5% is appropriate. * A target of <8.5% is appropriate for people with frequent, severe hypoglycaemia, advanced complications, older age or low life expectancy. * When HbA1c isn’t available, fasting plasma glucose targets of <7 mmol/l or post-prandial glucose of <9 mmol/l are appropriate for most adults.     Reflection question: How many of your patients have a personalized blood glucose target? |
| Some people with diabetes need to be referred to higher levels of care | * When creating a management plan for people with type 2 diabetes, it is important to assess a patient’s ability to provide self-care. * Some people (e.g. the elderly, people living with disabilities, isolated individuals and people with learning difficulties) may not be able to apply lifestyle changes or take medication as prescribed without support. These patients should be referred to specialist care. * Other criteria for non-emergency referral to higher levels of care are shown below. |
| Emergencies can arise when caring for people with diabetes | * Diabetes can sometimes present urgent, life-threatening situations that warrant emergency (same day) referral to higher levels of care. * It is important that people with diabetes and their families are aware of these medical emergencies, including how to recognize and avoid them. * Medical emergencies to be aware of are described in the box below.   **Diabetic ketoacidosis (DKA)** – a life-threatening complication that occurs when insulin levels are insufficient to allow cells to use glucose for energy. Instead, the liver breaks down fat, a process that produces ketones. Excess ketone levels turn the blood acidic, which is life-threatening.   * DKA is most common in people with type 1 diabetes. * Common causes include illness, missed insulin doses and insulin pump blockages. * Symptoms include intense thirst, frequent urination and changed mental state. High blood or urine ketone levels (0.6–1.5 mmol/l) may occur during illness. Very high levels (>1.6 mmol/l) can be indicative of DKA.   **Hyperosmolar hyperglycaemic state (HHS)** – a life-threatening complication of diabetes that occurs with extremely high blood glucose levels (often >40 mmol/l [720 mg/dl]) over a period of weeks resulting in severe dehydration. It is most common in people with type 2 diabetes. Symptoms are similar to DKA with intense thirst, frequent urination and changed mental status.  **Critical limb ischaemia** – markedly reduced blood flow due to a severe blockage in the arteries of the lower extremities. Presents as severe pain or numbness in the legs or feet while a person is not moving. Other symptoms include absent or diminished pulse in the legs or feet.  **Anuria** – the absence of urine production, defined as the production of fewer than 100 ml daily. |
| Diabetes management should focus on achieving glycaemic control while managing other cardiovascular risk factors | * As a complex disease, people with type 2 diabetes should ideally receive comprehensive care that aims to achieve glycaemic control while managing other cardiovascular risk factors such as hypertension and dyslipidaemia. * For cardiovascular disease prevention, statins are recommended for all people with type 2 diabetes older than 40 years, but only if this does not negatively impact access to glucose-lowering and blood pressure lowering medication. * Recommendations for managing hypertension are shown below.      * Where possible, diabetes care should include integrated management with other associated diseases such as cardiovascular disease and tuberculosis. * An agreed, person-centred and regularly reviewed diabetes care plan, including monitoring of glycaemic control and diabetes complications, are important aspects of the management approach. |
| Oral therapies in type 2 diabetes | Oral antihyperglycaemic agents should be considered if glycaemic targets are not achieved with lifestyle interventions alone | * Lifestyle interventions are essential for diabetes management. However, oral therapies should be considered if glycaemic targets are not achieved with lifestyle interventions alone in the first month following diagnosis. Additional agents might be required if one drug therapy is not sufficient to control blood glucose.      * Of the options available, metformin, empagliflozin (an SGLT2 inhibitor) and gliclazide (a sulfonylurea) are included in the World Health Organization’s (WHO) Model List of Essential Medicines. |
| Metformin is the first-line pharmacotherapy for treating type 2 diabetes | Metformin is recommended as first-line pharmacotherapy for type 2 diabetes due to its mild side effect profile, affordability, ease of administration and neutral-to-positive effects on body weight.  The HbA1c reduction with metformin is approximately 0.6% (5.5 mmol/mol) at 500 mg daily and 2.0% (22 mmol/mol) at 2,000 mg daily.  Metformin does not cause hypoglycaemia as it does not stimulate insulin secretion. Although metformin is generally well tolerated, it is associated with gastrointestinal side effects. To mitigate these side effects, metformin should be titrated slowly. |
| Many people with type 2 diabetes need dual or triple antihyperglycaemic therapy | * Metformin alone is not always sufficient to manage blood glucose, and dual therapy is often needed. * The WHO recommends the addition of a sulfonylurea if glycaemic targets are not achieved with metformin alone. A sulfonylurea might be used instead of metformin if contraindications are present. * Sulfonylureas are beginning to be replaced by newer glucose-lowering agents with a lower risk of hypoglycaemia, but due to their affordability they remain an important therapeutic option globally.      * Sodium-glucose cotransporter-2 (SGLT2) inhibitors are another class of oral antihyperglycaemic agents. The WHO recommend SGLT2 inhibitors as an add-on treatment for non-pregnant adults with, or at high risk for, cardiovascular disease and/or diabetic nephropathy. * Empagliflozin is the SGLT2 inhibitor included in WHO’s Model List of Essential Medicines.      * GLP-1 receptor agonists are increasingly recommended as first- and second-line therapies in high-income countries due to their high glycaemic efficacy, association with significant weight loss and cardiovascular benefits. Only one GLP-1 RA is available as an oral therapy. At present, GLP-1 RAs are not included in WHO treatment guidelines as they are infrequently available in low-income countries.   Reflection question: How many of your patients are treated with metformin as monotherapy? Are they achieving their glycaemic targets? |
| Injectable therapies for diabetes | Treatment with insulin should be initiated in people with type 2 diabetes if blood glucose is not well managed with dual oral therapy | * Intermediate-acting insulin NPH is recommended by WHO as third-line pharmacotherapy if blood glucose targets are not achieved with dual oral therapy. * If insulin treatment is unsuitable (e.g. people who need support with injections but live alone), a DPP-4 inhibitor, SGLT2 inhibitor or thiazolidinedione can be added.      * Long-acting insulin analogues should be used in people who experience frequent, severe hypoglycaemia with intermediate-acting insulin. * Intermediate- and long-acting (basal) insulin is not matched to food and does not require patients to have an understanding of carbohydrate counting. * Long-, rapid- and short-acting insulin should be initiated in higher levels of care. |
| Insulin is administered via subcutaneous injection | * People with type 2 diabetes who require insulin should be educated on appropriate insulin administration. * Insulin should be injected into fatty tissue at a 90o angle. The main injection sites are usually stomach, thighs, buttocks and arms. * Intramuscular injection should be avoided as this may result in more rapid absorption and serious hypoglycaemia.      * To avoid bumps and scar tissue on the skin (lipohypertrophy), which can cause discomfort and poor insulin absorption, injection sites should be rotated. A systematic approach to injection site rotation should be adopted, with each injection at least 2.5 cm away from the previous.      * When administering intermediate-acting (NPH) insulin, injection locations should be tailored to time of day.   + In the morning, NPH should be given in the abdomen to increase speed of absorption in order to cover post-breakfast glycaemic excursions.   + In the evening, NPH should be given in the thigh or buttock as this leads to slower absorption and decreases the risk of nocturnal (overnight) hypoglycaemia. * The shortest available needles are preferred for all patients. This is 4 mm for pen injectors and 6 mm for insulin syringes. * Reuse of needles and syringes is not recommended but may be necessary in some circumstances. Patients should be advised to discard needles when injections become more painful or after a maximum of 5 uses. * All people with diabetes treated with insulin should have a safe means of needle disposal. * People with type 2 diabetes may be resistant to starting insulin therapy. They may be reluctant to inject themselves or may be fearful of hypoglycaemia. These factors should be explored and addressed to achieve good treatment adherence. * Watch Dr SP Chan explain how to initiate insulin therapy.   **<<INSERT VIDEO HERE >>** |
| Patients require education on the need to store insulin carefully to maintain potency | * Insulin should be dispensed with very clear instructions regarding its transportation from the health facility to the home and its safe storage and use at home. |
| Monitoring people with diabetes | Self-monitoring of blood glucose should be available to people with diabetes, where possible | * WHO recommends that all people with diabetes have access to blood glucose monitoring at home. This is particularly important for people with diabetes treated with insulin who, in some circumstances, can be educated on independent dose adjustment for optimal management. * Individuals with the ability to carry out regular blood glucose monitoring at home should be aware of their target blood glucose levels. * Self-monitoring of blood glucose is also important to detect hyperglycaemia or hypoglycaemia early.   Reflection question: How many of your patients have access to blood glucose monitoring at home? How many of those treated with insulin are able to self-monitor? |
| Hyperglycaemia should be detected and managed promptly to avoid adverse health complications | * Hyperglycaemia, or high blood sugar, is associated with the development of diabetes-related comorbidities. Hyperglycaemic complications cause significant morbidity and mortality and constitute a large burden for people with diabetes, their relatives and healthcare systems. * It is important to monitor blood glucose levels and respond quickly to hyperglycaemia. * Ideally, hyperglycaemia should be detected and managed before symptoms arise. Because this is not always possible, the symptoms to be aware of are outlined below.      * People with diabetes who experience frequent hyperglycaemia or symptoms of hyperglycaemia should report to their healthcare professional for treatment adjustment. * Acute hyperglycaemic complications include DKA (most common in type 1 diabetes) and HHS (most common in type 2 diabetes), which are medical emergencies. |
| People with diabetes may experience hypoglycaemia and should be aware of symptoms and treatment | * Hypoglycaemia, or abnormally low blood glucose, is a major reason for morbidity in people with diabetes. It is a cause of worry for people with diabetes and their families. * People with diabetes should be counselled on the causes of hypoglycaemia, and how to recognize, prevent and treat it. * Hypoglycaemia is caused by excess insulin, which can occur in people treated with exogenous (injected) insulin or insulin secretagogues (sulfonylureas) that increase insulin secretion from beta cells. * It can also be induced by factors such as fasting, alcohol consumption, changes in diet, exercise or temperature, among others, which cause changes to insulin.      * People treated with insulin and/or insulin secretagogues should have access to blood glucose monitoring equipment and be educated on how to safely treat hypoglycaemia. * Hypoglycaemia needs to be treated quickly to prevent progression to severe hypoglycaemia. |
| Meet Amari, a 64-year-old man with type 2 diabetes | *Let’s reflect on what we have learnt so far in this chapter and begin to put learnings into practice.*    Amari is a 64-year-old man with type 2 diabetes diagnosed 3 months ago with a fasting plasma glucose of 7.9 mmol/l (142 mg/dl) and obesity, but no other comorbidities. At diagnosis, you counselled him on the importance of early intervention and lifestyle changes in managing type 2 diabetes. You discussed Amari’s current diet, advising him to reduce sugar and saturated fat. You also encouraged him to increase his physical activity to 30 minutes of moderate intensity exercise each day. Three months later, Amari returns to clinic for a review.  Vital signs  Weight: 119 kg  Height: 183 cm  BMI: 35.5 kg/m2  Fasting plasma glucose: 7.9 mmol/l  HbA1c: 7.2% (55 mmol/mol)  **Family history**  Father suffered a myocardial infarction aged 74.  **Reflection questions**   * What blood glucose target is appropriate for Amari? * Based on recommendations from the WHO, when would you start pharmacotherapy for Amari? * What would you select as the first-line therapy? * How would you initiate this treatment to reduce the likelihood of side effects? * When would you review Amari to assess the effectiveness of his treatment plan?   **Now that you have reflected on these questions, see below for an example of how you could respond.**  Amari is relatively young and healthy with no diabetes complications. Currently he is not treated with any medications that could cause hypoglycaemia, so a glycaemic target of <6.5 mmol/l (126 mg/dl) would be appropriate.  Amari’s current FPG is above the threshold for initiation of oral therapies. Prompt treatment is important to minimize risk for developing complications of diabetes, so initiation of metformin, the recommended first line medication, should not be delayed. Metformin should be titrated slowly to prevent gastrointestinal side effects. The WHO recommend starting with 500 mg metformin once-daily, taken with a meal and increasing the dose by 500 mg at 3-monthly intervals. Amari should be reviewed in 3-months to assess his response to metformin treatment, or earlier if symptoms occur. |
| Special considerations for managing diabetes | People with diabetes need additional support managing concurrent illness | * Occasional sickness is a natural part of life but confers additional complications for people with diabetes. * As part of the body’s defence mechanism for fighting illness and infection, more glucose is released into the bloodstream. Illness and infections can, therefore, raise blood glucose levels to dangerously high levels. * People with diabetes need education on managing sick days to prevent complications such as diabetic ketoacidosis and/or hyperosmolar hyperglycaemic state. |
| Religious and cultural considerations can impact diabetes management | * Diabetes treatment plans should be tailored to the individual. This includes offering support and personalization based on religious and cultural considerations. * Many people choose to fast for religious reasons such as Ramadan.   Reflection question: How many of your patients choose to fast for Ramadan? Are you offering support for your patients during this time?   * Ramadan marks a sudden shift in mealtimes, sleep and wakefulness patterns, leading to physiological changes in homeostatic and endocrine processes. * Although individuals with diabetes are exempt from fasting during Ramadan, data suggests that 42.8% of people with type 1 diabetes and 78.7% of people with type 2 diabetes globally choose to fast for at least 15 days during Ramadan. * Because fasting is common during Ramadan, people with diabetes need to know how to fast safely, reducing the risk of hypoglycaemia, hyperglycaemia and dehydration. * People with diabetes intending to fast should be:   + assessed for hypoglycaemia awareness   + given means of self-monitoring blood glucose values   + advised on diet and fluid intake   + educated on how to break the fast safely and when to break the fast early   + aware of how to tailor their treatment to avoid hypoglycaemia or hyperglycaemia during fasting. |
| Family planning and preconception care is an important part of diabetes management | * Diabetes in pregnancy is associated with an increased risk of adverse outcomes for mother and baby.      * Women with diabetes require extra support before conception and during pregnancy to achieve optimal glycaemic management and reduce the likelihood of adverse outcomes. Effective pre-conception care significantly reduces the risk of adverse pregnancy outcomes.     Reflection question: Do you review contraception and pregnancy plans with women of childbearing age with diabetes during routine appointments?   * Pre-pregnancy care should begin at least 3–6 months before conception to allow for meaningful change to glycaemic control. Effective contraceptive methods should continue to be used during this time. * People with diabetes who are hoping to conceive should aim to achieve blood glucose levels as close to normal as possible, without significant hypoglycaemia. A target HbA1c of <6.5% (48 mmol/mol) is appropriate. * Pre-pregnancy care should include lifestyle advice and a review of medications. |