PEER REVIEWED

Palliative and end-of-life care for patients with diabetes

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Diabetes complications are common and can contribute to unpleasant symptoms, depression and reduced quality of life. A palliative approach to diabetes care in patients with complications, including modified metabolic targets, can reduce symptoms and hospital admissions and improve quality of life and care transitions. GPs have a key role in co-ordinating palliative and end-of-life care in these patients.

Key points

- **Palliative care aims to improve comfort and quality of life, optimise function and help patients make decisions about their end of life.**
- **A palliative approach can start early in the course of diabetes care for patients with complications and comorbidities and can be combined with active diabetes treatment.**
- **Key strategies in palliative care for people with diabetes include modifying glycaemic targets, minimising hyperglycaemic and hypoglycaemic episodes, managing medicines (particularly diabetogenic medicines), maintaining nutrition and hydration, and supporting family and carers.**
- **The Gold Standard Prognostic Indicator and assessment of the end-of-life stage can help GPs determine life expectancy, which can aid GPs, patients and their carers in deciding when to withdraw treatment.**

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Palliative care refers to care that improves the quality of life for people living with a life-threatening or incurable chronic disease and their families. The focus is on relieving suffering by identifying problems early, undertaking a thorough assessment and engaging the individual and family carers in care decisions.[1] Palliative care can be combined with life-maintaining treatment and is particularly relevant to people with diabetes and associated complications, such as cardiac disease, end-stage renal disease and nonhealing diabetic foot disease, when remediable surgery and other treatments are ineffective.

End-of-life care refers to care for people likely to die in the following 12 months. This includes patients with progressive incurable diseases, frailty, acute life-threatening illnesses and diseases that can cause sudden death (such as diabetes), as well as those whose death is expected in a few hours to days.[2] End of life is often divided into four inter-related stages: stable, unstable, deteriorating and terminal.[3] These four stages are not linear, especially in people with diabetes who often have many stable and unstable periods before they deteriorate towards the terminal stage.[3]

A palliative approach in diabetes

A palliative approach can be integrated with usual diabetes management, for example for patients with end-stage renal disease receiving dialysis and those with heart failure or advanced neuropathic disease. Significantly, the early addition of palliative care in such situations improves comfort and quality of life, gives people a sense of control over their lives and can be a responsibility shared between the individual and their family, the GP and palliative and diabetes specialists.[4]

As a more palliative approach is adopted, the focus changes from tight blood glucose control to symptom control. The usual diabetes management plan and metabolic targets often need to be revised

with the aim of promoting comfort, improving quality of life and limiting hypoglycaemia and hyperglycaemia. These revisions should suit the individual's health and functional status, medicine regimen, risk profile and life expectancy.

Deciding when to stop medicines and withdraw other treatment is challenging. GPs can help patients with diabetes to work through these issues and to document their care preferences, thereby providing valuable information for palliative and diabetes specialists. Preventing hypoglycaemic and hyperglycaemic episodes is an important aspect of promoting comfort and quality of life. Importantly, the care plan must be developed with the individual and usually their family carers.

Planning for end of life

Planning for end-of-life care goals needs to be discussed and documented early in the palliative journey and then reviewed regularly because people's preferences can change over time and with transitions of care such as admission to a residential aged care facility. Many people prefer to die at home, but home deaths can be particularly challenging and burdensome for the family.[4] It is essential to consider people's spiritual and cultural beliefs and values and the care of the body after death when discussing end-of-life care.

A key difficulty for many health professionals, including GPs, is discussing palliative and end-of-life care when the prognosis is unpredictable. However, having documented advanced care directives can reduce patient anxiety and improve quality of life and satisfaction for patients and their families as well as providing guidance for clinicians at the end of life.

Key management strategies

Diabetes is one of the most common comorbidities in palliative care situations, but optimal diabetes management in palliative and end-of-life care is largely based on expert opinion, retrospective studies, surveys and interviews.[5] Consequently, the following diabetes management strategies, although derived from the best available evidence, are primarily consensus recommendations informed by the clinical experience of palliative and diabetes experts. Practice points for GPs on palliative and end-of-life care for people with diabetes are summarised in Box 1.

1. Practice points for GPs on palliative and end-of-life care for patients with diabetes

General practice points

- It is important to understand a patient's preferences to ensure palliative and end-of-life care plans suit their wishes; cultural beliefs, attitudes and values must be considered.
- Palliative care is a broader concept than end-of-life care; it refers to a care approach that improves comfort and quality of life and optimises function as well as helping patients make decisions about their end of life.
- Patients should be encouraged to continue to be active within their functional limitations.

Diabetes-specific practice points

- A palliative approach can start early in the course of diabetes care and can be combined with active diabetes treatment.
- Symptoms that cause distress are multifactorial; hyperglycaemia or hypoglycaemia could be underlying causes, contributory factors or consequences and can be identified with blood glucose testing.
- Cachexia is common in people with diabetes and cancer. Nutrition and other approaches such as exercise should aim to maintain muscle mass and function.
- The medicine regimen and doses may need to be tailored to the individual's health status.
- Diabetes management goals should be considered in light of the Palliative Care Outcomes Collaborative (PCOC) end-of-life stages (stable, unstable, deteriorating and terminal) and life expectancy.
- Planning for end-of-life care is an essential aspect of diabetes care and should not be left to the last stages of life. Early planning helps the individual think through their choices for future care while they are able to make informed choices.
- People with diabetes and family carers require specific education about the care plan when a palliative approach is implemented and as the management goals change.
- Corticosteroid-induced diabetes is common and under-recognised. Individuals at high risk of diabetes should be screened and hypoglycaemic medications commenced if indicated.
- Assessing the need for palliation and end-of-life care planning can be incorporated into the annual cycle of diabetes care.

Modifying glycaemic targets

People with type 1 diabetes require insulin, even when the aim is not to achieve tight glycaemic control. In addition, as type 2 diabetes is associated with a progressive loss of beta cell function and declining insulin production, over 50% of people with type 2 diabetes eventually need insulin. The need for insulin may be greater in palliative care and at the end of life, especially when diabetogenic medicines are used and when other factors, such as pain, contribute to hyperglycaemia and symptom burden.

Although preventing long-term diabetes complications is not a priority of palliative and end-of-life care, managing existing complications and comorbidities to relieve pain and prevent unnecessary presentations to the emergency department or admissions to hospital is important, especially during the stable and unstable end-of-life phases. Insulin may help address these goals and reduce the medicine burden. GPs are in an ideal position to detect changes in the stable and other end-of-life phases and implement timely appropriate care or make an early referral to diabetes and palliative specialists.

The optimal blood glucose and glycosylated haemoglobin (HbA_{1c}) ranges in palliative care and at the end of life are unclear. It is, however, clear that the target ranges need to be individualised to suit the

2. Confusion Assessment Method for detecting delirium[8]

Rate the criteria 1 to 4 as 'yes' if present and 'no' if not present. If the patient scores 'yes' for criteria 1 and 2 and 'yes' for either criterion 3 or 4 then the screen indicates delirium is present but may not indicate the underlying cause(s).

Criteria	Comment
1. Acute onset and fluctuating course	Score yes if the person has an acute change in mental status from usual (baseline)
2. Inattention	Score yes if the person is easily distracted or has difficulty following the conversation
3. Disorganised thinking	Score yes if the person's conversation rambles, is illogical or unpredictably changes the subject
4. Altered level of consciousness: hyperactive or hypoactive	Score yes if the person is vigilant, lethargic or stuporous, or in a coma

patient's health status, comfort and likely prognosis. Recent guidelines recommend:

- blood glucose targets of 6 to 8 mmol/L fasting and 6 to 11 mmol/L postprandial, avoiding levels less than 6 mmol/L and over 15 mmol/L
- HbA_{1c} levels up to 8% for most people.[6,7]

Likewise, the frequency of blood glucose monitoring in palliative and end-of-life situations varies between guidelines, but there is an increasing consensus that the care plan must be individualised. The frequency should be based on clinical judgement and tailored to suit the individual, and may change as the person's health status changes. Health professionals often debate the value of blood glucose testing at the end of life, but many people with diabetes and their families regard it as an important component of self-care and a familiar task in a sometimes rapidly changing situation.

Minimising hyperglycaemia

Hyperglycaemia is not a benign condition. It causes or exacerbates distressing symptoms such as thirst, urinary frequency and tiredness, and contributes to some forms of pain, such as headache, abdominal pain in ketoacidosis and in the longer term, neuropathic pain. The last is a significant problem and is usually not relieved by opioids.[5]

In addition, hyperglycaemia can cause delirium and confusion, which affects the individual's ability to problem-solve and cope, lowers mood and compromises quality of life. It is important to diagnose delirium and differentiate it from depression and behavioural changes associated with hypoglycaemia. Delirium causes significant morbidity in people with cancer, advanced heart disease and renal, hepatic and pulmonary disease and is associated with falls in hospital.[5] Some medicines, such as opioids, corticosteroids, anticholinergics and benzodiazepines in older people, predispose patients to delirium.[5] Regular blood glucose testing, hypoglycaemia risk screening and screening for confusion, for example using the Confusion Assessment Method (Box 2), can help detect delirium early and flag the need for further assessment to determine the likely cause.[8]

Hyperglycaemia can be present without the classic symptoms and thus can be missed and go untreated, allowing progression to ketoacidosis in patients with type 1 diabetes or hyperosmolar states in those with type 2 diabetes. Both these conditions are life-threatening and require urgent care; they can be detected by blood glucose testing. A key role of the GP is to determine when hyperglycaemia is preventable and remediable and not a signal of the beginning of the dying phase.

Minimising hypoglycaemia

Hypoglycaemia is a significant risk for people using insulin and some other hypoglycaemic medications, and the risk can vary with changing health status. Proactively determining hypoglycaemia risk and regularly reassessing this risk helps reduce the number of hypoglycaemic episodes (see Box 3).[9] Importantly, hypoglycaemia affects delayed and working memory in the short term; therefore, like hyperglycaemia, it affects patients' decision-making and problem-solving capacity.[10,11] Severe hypoglycaemia leads to neuroglycopenia (low glucose level in the brain), which can contribute to confusion and delirium. Severe hypoglycaemia can also trigger myocardial infarction and sudden death.

The impact of hypoglycaemia and hyperglycaemia on cognitive function and decision-making indicate that end-of-life care choices should be discussed when the patient's blood glucose level is in the optimal range. It is important to realise that circulatory deficits and hypotension may affect the accuracy of capillary blood glucose tests because less glucose reaches peripheral tissues.

Treating hypoglycaemia is difficult when patients have cachexia, anorexia, nausea, vomiting or swallowing difficulties and cannot consume oral glucose. Cachexia is also associated with low glucose stores in muscle and the liver. Dramatic weight loss can contribute to hypoglycaemia and should trigger a review of hypoglycaemic medications. In addition, the counter-regulatory response to low blood glucose level that releases glucose from muscle and the liver becomes ineffective over time.[10]

However, it might not be appropriate to cease hypoglycaemic medications, except in the deteriorating and terminal stages at the end of life, because of the adverse effects of hyperglycaemia. Using hypoglycaemic medications with the lowest hypoglycaemia risk at the lowest effective dose is advisable. This can be achieved with small doses of rapid-acting insulin with meals and a small dose of a long-acting insulin analogue in the morning or at night. Conversely, weight loss can reduce insulin resistance and hyperglycaemia.

Managing medicines

Pharmocovigilance is essential in palliative and end-of-life care to achieve acceptable glycaemic targets and minimise hyperglycaemia, hypoglycaemia, other medicine-related adverse events and the medicine burden. GPs are ideally situated to undertake regular medicine reviews or refer individuals for a pharmacist medicine review. All reviews should include complementary and self-prescribed medicines because people with diabetes and people receiving palliative care frequently use complementary medicines. It is important to cease taking medicines when possible, to reduce polypharmacy and the medicine burden (e.g. statins). Nonmedicine options can be considered if appropriate, such as massage and acupuncture to manage pain.

Managing diabetogenic medicines and corticosteroid-induced diabetes

Commonly prescribed diabetogenic medicines include antipsychotics, thiazide diuretics and corticosteroids such as dexamethasone and prednisolone. Corticosteroids are commonly prescribed in palliative care (30 to 60% of patients) to manage anorexia, weight loss and fatigue, as well as conditions such as tumour-associated oedema and spinal cord compression.[12]

However, corticosteroids can mask the signs and symptoms of infection, which are often atypical in people with diabetes. The skin can become thin and fragile and prone to tears, especially in older people, which can cause considerable discomfort and distress. Corticosteroids also have variable effects on bone formation and reduce calcium absorption, which increases the risk of osteoporotic fractures and pain with long-term use. Corticosteroid-related mental changes range from mild psychosis to significant psychiatric pathology and can be difficult to distinguish from delirium and other cognitive changes.

GPs can determine the risks and benefits of corticosteroid use in palliative care by assessing:

- the patient's susceptibility to hyperglycaemia (including screening people without diabetes for diabetes risk factors)
- the proposed corticosteroid dose and regimen
- the diabetogenic effects of individual corticosteroids (including selecting the least diabetogenic medicine and using it for the shortest possible time, although high doses are often needed at the end of life)
- the optimal time to test blood glucose level, which typically increases in the afternoon.

The choice of hypoglycaemic medications for patients with corticosteroid-induced diabetes depends on the patient's health status, corticosteroid regimen and relevant medicine precautions and contraindications. The target ranges for blood glucose level are fasting around 6 mmol/L and postprandial less than 11 mmol/L. When ceasing a corticosteroid, the dose needs to be reduced slowly, while also gradually reducing the dose of hypoglycaemic medications to prevent hypoglycaemia. Blood glucose testing is an important guide to the doses of hypoglycaemic medications required in this situation.

3. Common causes and risk factors for hypoglycaemia in people with diabetes in palliative care and at the end of life

Medicine-related causes

- Prescribed hypoglycaemic medications, especially sulfonylureas and insulin
- Medicines that interact with hypoglycaemic medications, including some herbal medicines, such as bitter melon (*Momordica charantia*), gymnema (*Gymnema sylvestre*) and American ginseng (*Panax quinquefolius*)
- Prescribed medicines that reduce appetite or cause nausea and vomiting
- Renal disease, which is a common diabetes complication that affects medicine excretion and sometimes necessitates dialysis; macroalbuminuria predicts hypoglycaemia[15]
- Liver disease, which can affect medicine metabolism

Nonmedicine-related causes

- Weight loss, malnutrition and cachexia, which affect glucose stores and reduce the ability to mount a counter-regulatory response (present in 40 to 90% of the cancer palliative care population)
- Hypoglycaemia unawareness, which is common in older people and those with type 1 diabetes caused by autonomic neuropathy and affects production of some counter-regulatory hormones (e.g. glucagon)
- Cognitive impairment and delirium, which could result from chronic hypoglycaemia, hyperglycaemia, medicines or dementia or a combination
- Unmanaged pain, which can affect appetite
- Fasting for procedures or surgical interventions
- Health professionals and family carers mistakenly attributing hypoglycaemic or hyperglycaemic coma to other causes, such as the dying process

It is important that palliative care clinicians inform GPs about the reason for prescribing corticosteroids, proposed duration of use and weaning procedure so that the GPs can support and monitor appropriate use and patient education.

Maintaining nutrition and hydration

Nutrition advice can help the patient, GP, family and other carers decide on an acceptable nutrition regimen that limits malnutrition and minimises weight loss and its consequences, such as loss of muscle mass. Reversible causes of anorexia and weight loss, such as dysphagia, depression, nausea and malabsorption, need to be identified and treated if possible. However, the metabolic processes involved in wasting due to cachexia and sarcopenia in palliative care situations are complex, vary between different disease processes, differ from cancer-related cachexia and are generally

irreversible in advanced disease. GPs should refer patients receiving palliative or end-of-life care to a dietitian and/or palliative specialist for specific nutrition advice.

In addition, people with diabetes are often deficient in essential nutrients and may have anaemia associated with renal disease and metformin use. Anaemia contributes to tiredness, and some forms of anaemia can lead to artefactually low HbA_{1c} levels.

People with cachexia may require supplements (e.g. protein), especially in the stable and unstable end-of-life stages. When people can no longer consume adequate food and fluids orally, enteral feeds might be required to sustain energy reserves and provide essential nutrition and fluids, but the risks and benefits need to be considered.

Supporting family and carers

Changes in care goals from tight blood glucose control to a focus on comfort and symptom management can be challenging for patients and their families and other carers. GPs are ideally placed to explain that the changes do not mean clinicians are 'giving up on them' and to support patients and their families to decide their care goals and to document their end-of-life care preferences.

Some family and carers require education and written information about how to perform diabetes self-care tasks such as blood glucose monitoring and administering insulin when the person with diabetes is no longer able to perform diabetes self-care.

It can be very stressful witnessing a loved one suffer, and thus it is essential that GPs consider the health and wellbeing of the carers during the palliative and end-of-life journey and after their loved one dies. Caring is associated with an increased risk of myocardial infarction in the months after a family member dies, and carers often have stress-induced immunodeficiency.[13,14]

Withdrawing treatment

Knowing the prognosis helps GPs, people with diabetes and their carers decide when to withdraw treatment. Patients should document their preferences in their end-of-life care plan. The Gold Standard Prognostic Indicator and assessment of the end-of-life stage can help GPs determine life expectancy.[2] The following factors are associated with short life expectancy:

- multiple comorbidities
- losing more than 10% of body weight in a short period of time
- general decline or 'failure to thrive'
- serum albumin level less than 25 g/L
- declining functional status (e.g. score on the Karnofsky Performance Status Scale less than 50%)
- requiring significant help to perform the usual activities of daily living and diabetes self-care tasks
- loss of 'the will to live'; this will is a strong predictor of survival in older people, regardless of their age, sex and comorbidities, and is influenced by social factors such as satisfaction and support from family, friends and health professionals.[15]

Conclusion

GPs play a central role in optimising care for people with diabetes requiring palliative and end-of-life care and in supporting their families. GPs are in an ideal position to identify changes in the end-of-life stage and their likely significance, and also provide an essential link to palliative care and diabetes specialists and facilitate continuity of care, including care for families after the death of the patient. **ET**

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