

The Palliative Care Handbook

Guidelines for clinical management
and symptom control, featuring extensive
support for advanced dementia



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Miscellaneous

Diabetes, hyperglycaemia and hypoglycaemia.....

The pathophysiology of diabetes in the palliative care setting (and particularly in the terminal phase) may be complex as the control of blood sugar may be lost due to insulin resistance associated with illness and also because of erratic nutritional intake.

- certain malignancies e.g. pancreatic cancer also affect the beta cells directly
- control of blood glucose concentrations is important in palliative care as both hyperglycaemia and hypoglycaemia may cause symptoms resulting in a loss in the quality of life
 - e.g. marked hyperglycaemia may exacerbate pre-existing cachexia - in the catabolic state insulin has an anabolic effect
- management must balance treatment tolerability (including tolerability of blood glucose monitoring if required) with treatment efficacy and symptom control

Diabetes

Type 2 diabetes (previously called non insulin dependent diabetes [NIDDM])

- tight control of blood glucose concentrations is not necessary, although if it is easily achievable it may increase quality of life
- relax usual dietary restrictions and adjust insulin/hypoglycaemic agent use as appropriate
- if the patient is taking metformin consider discontinuing it to avoid the adverse effects of metformin e.g. nausea, weight loss and lactic acidosis. There may be a need to add a different drug e.g. insulin
- if the patient is taking a dipeptidyl peptidase inhibitor e.g. sitagliptin this may be continued but other 'third line' antidiabetic agents can be discontinued e.g. pioglitazone, dapagliflozin, acarbose
- weight loss reduces blood glucose concentrations so requirements for antidiabetic agents may reduce as weight is lost
 - once weight loss begins or appetite decreases, halve the dose of antidiabetic agent in previously well controlled patients
 - reduce doses further or stop as required
- on admission to a hospice, oral hypoglycaemic agents i.e. sulphonylureas will not be required unless there is an infection or other serious stress in which case
 - monitor blood glucose concentrations every 2 days (after the main meal if possible) and treat hyperglycaemia if symptomatic
- symptoms of hyperglycaemia will usually appear at blood glucose concentrations of > 15 mmol/L so treatment should begin only above this concentration (in the near terminal phase, may consider treatment if blood glucose > 20-25 mmol/L)
 - avoid HYPOGLYCAEMIA during this treatment as it may be difficult to reverse without systemic therapy especially if the patient is vomiting or not eating

- give a fast acting insulin analogue e.g. lispro (Humalog™), aspart (NovoRapid™) or glulisine (Apidra™) insulin 2 to 4 hourly initially (usually for 24 hours) in doses determined by monitoring - usually 5 to 10 units BUT tailor dose to both the size of the patient and food intake
- once in the range 10 to 15 mmol/L convert to an intermediate or long acting insulin e.g. isophane insulin (Protaphane™) or glargine (Lantus™) once or twice daily injections at 75% of the 24 hour short acting dose. Chart a fast acting insulin analogue e.g. lispro (Humalog™) or glulisine (Apidra™) insulin to be used for breakthrough hyperglycaemia (post-prandially if eating).
- monitor fasting blood glucose concentrations daily for several days then twice per week
- discuss management with the patient to avoid misinterpretation

Type 1 diabetes (previously called insulin dependent diabetes [IDDM]) – these are the minority of patients who are on insulin.

- insulin must be continued even in the terminally ill to avoid diabetic ketoacidosis. Consider capillary beta hydroxyl-butyrate monitoring if > 1.2 mmol/L ketosis is likely and should be treated if appropriate
- tight control is not necessary
 - a blood glucose concentration of 10 to 15 mmol/L is a good target unless patient is symptomatic
- if the patient is well nourished and has a steady oral intake negotiate with the patient (or substitute decision-maker) re the following
 - maintain the usual dose of insulin
 - monitor blood glucose concentrations twice a day every 3 days
 - when appetite decreases, increase blood glucose concentration monitoring and decrease insulin
- if patient is vomiting, is no longer eating or has a variable appetite
 - use a base line long acting insulin e.g. glargine (Lantus™) daily and chart a fast acting insulin analogue e.g. lispro (Humalog™) or glulisine (Apidra™) insulin to be used for breakthrough hyperglycaemia (post-prandially if eating)
 - monitor frequently
- if the patient is near to death
 - discuss continuation of insulin with patient and family

Hyperglycaemia

Symptoms

- at blood glucose concentrations of < 15 mmol/L
 - major symptoms are rare
- at blood glucose concentrations of 15 to 40 mmol/L
 - dehydration, dry mouth
 - thirst
 - polyuria
 - lethargy
 - blurred vision

- candidiasis
- skin infection
- confusion
- at blood glucose concentrations of > 40 mmol/L
 - drowsiness
 - obtundation
 - coma

NB Some of these symptoms may be present in terminally ill patients in the absence of high blood glucose concentrations.

Causes

- in diabetic patients
 - lack of insulin or hypoglycaemic agent
 - loss of dietary control
 - stress, illness
 - infection
 - myocardial infarction
 - GI motility disorders and obstruction
- in non-diabetic patients
 - malignant disease
 - > over 1/3rd of cancer patients will develop Type 2 diabetes (NIDDM) - an effect on metabolism
- drugs (even in non-diabetic patients)
 - corticosteroids e.g. dexamethasone, prednisone
 - diuretics (at high dose) e.g. bendrofluazide, frusemide

Management

- in active palliative care patients
 - closely monitor blood glucose concentrations as this may help them to retain function
- in patients who are close to death
- aim for minimal monitoring and maximal comfort
 - treat the patient rather than blood glucose concentration
 - aim for maximum quality of life by loosening control of blood glucose and encouraging eating if appropriate
- in Type 2 diabetes (non-insulin dependent) patients
 - often rehydration will partially reverse hyperglycaemia
 - BUT insulin (often only once a day) may be necessary
- in Type 1 diabetes (insulin dependent) patients
 - give insulin at least twice a day (continue with patient's usual regimen if possible) basing the dose on body weight and predicted carbohydrate intake
 - withdrawal of insulin in these patients will lead to diabetic ketoacidosis (acidosis, shock then death), often over a period of hours or days

- if diabetic ketoacidosis occurs treat with rehydration and iv insulin if appropriate
- drug related monitoring of blood glucose
 - corticosteroids e.g. dexamethasone, prednisone
 - > often cause hyperglycaemia
 - > any patient who has taken them for longer than 3 weeks should have intermittent blood glucose concentration monitoring
 - > diabetic patients taking them should have more intense blood glucose monitoring depending on the prognosis
 - ~ monitor fasting blood glucose concentrations daily for a week then 3 times a week for 3 weeks or until stable then weekly
 - ~ in terminal patients take a fasting blood glucose concentration every 2 days for one week and then according to clinical status

Hypoglycaemia

Symptoms - CNS

- behaviour changes, anxiety, aggression
- confusion
- fatigue
- seizures
- loss of consciousness

Symptoms - peripheral

- palpitations
- tremor
- sweating
- hunger
- paraesthesia
- pallor
- increased heart rate

Causes

- diseases
 - insulinomas (rare)
 - autoimmune disease (rare)
 - infection (sepsis)
 - carcinoid (rare)
- failure to adhere to good glucose monitoring technique
- organ failure
 - renal, hepatic, cardiac
- diet - low food intake
- drugs
 - insulin

- hypoglycaemic agents e.g. glipizide
- alcohol
- quinine
- pentamidine

Management

- treat/remove causes where possible
- give glucose (oral or iv), glucagon
- monitor blood glucose concentrations

Using steroids.....

Steroids are often seen as cure-all/miracle drugs in palliative care. Careful consideration should be given to initiating these drugs as they have many adverse effects. Most of the use in palliative care is for unlicensed and/or non-evidence based indications e.g. spinal cord compression, nerve compression, dyspnoea (from a number of causes), SVC obstruction and inflammation following radiation therapy, pain relief, anti-cancer hormone therapy, appetite stimulation and the enhancement of wellbeing.

Adverse effects

- diabetes mellitus
- osteoporosis
- avascular bone necrosis
- mental disturbances
 - insomnia, paranoid psychosis, depression, euphoria
- muscle wasting (predominantly proximal myopathy)
- peptic ulceration - not as severe as NSAID induced ulceration but of concern particularly in the elderly or patients with other risk factors
- skin thinning
- immunosuppression
 - infection - candidiasis, septicaemia
 - poor wound healing
- sodium and water retention - leading to oedema
- potassium loss
- hypertension
- Cushing's syndrome
 - moon-like face
 - striae
 - acne

Prescribing

- a trial of 5 days at 4 to 16 mg dexamethasone (dose dependent on indication) should be considered after benefit/risk has been assessed and discussed
 - dexamethasone is the preferred drug - prescribe as a single or 2 morning doses (before noon) to avoid sleep disturbance
- consider gastric protection with a PPI e.g. pantoprazole particularly in the elderly
- consider blood glucose monitoring (particularly if continuing)
- higher doses may be required if the patient is taking CYP enzyme inducers e.g. phenytoin and lower doses with inhibitors e.g. fluconazole
- withdraw completely if used for less than 2 weeks and < 6 mg dexamethasone. Otherwise tail off by 2 mg every 5 to 7 days until 2 mg once daily, then by 0.5 mg every 5 to 7 days

The last days or hours.....

Recognising the ending of a life may seem relatively easy or obvious but in practice the 'diagnosis of dying' may be challenging for individuals or teams. Signs may include:

- the patient becoming increasingly weak, sleepy, disinterested in getting out of bed, seeing anyone other than close family, less interested in surroundings, confused or agitated
- symptoms becoming more apparent and physical changes suggesting the body closing down becoming more noticeable (skin colour changes, skin temperature changes, slowing of respiration or Cheyne-Stokes respiration, involuntary twitching or moaning)

Management

- planning for the death is important
- if in an institution ensure that advance care plans indicate that the person is not for resuscitation
- ensure cultural or religious wishes are known and followed
- ensure that the patient and family are aware of the progression of disease and let them know what you expect to happen
- much anxiety near the end-of-life is engendered by a fear of the unknown so provide information about those things that are known to mitigate feelings of uncertainty
- anticipate what might happen rather than wait for a crisis
- anticipatory prescribing is considered to be best practice - analgesics, antiemetics, anxiolytics and antisecretory drugs should all be considered remembering that the oral route will probably be lost so use the subcut route

Common symptoms

Pain (see pain section)

opioids are the predominant analgesics used

- if the oral route is not feasible then consider
- fentanyl patches - not suitable for unstable pain but may be useful as an alternative to oral analgesic
- subcut boluses prn or continuous infusion

- conversion from oral to subcut is 2:1 for morphine and oxycodone i.e. 10 mg oral = 5mg subcut

Nausea/vomiting (see nausea/vomiting section)

- not usually a great problem unless there is intestinal obstruction or it has previously not been controlled

Agitation/distress/anxiety (see fear, anxiety, delirium sections)

Non-pharmacological management

- if there are fears/worries/tensions/spiritual issues consider what has helped in the past
- consider and address constipation/urinary retention/pain

Oral/buccal drugs

- lorazepam tablets 0.5 mg to 1 mg bd
- clonazepam drops (2.5 mg/mL - 0.1 mg per drop)
- midazolam sublingually or buccally (between gum and cheek)

Subcutaneous drugs

- midazolam 10 mg over 24hrs is a usual starting dose if not on benzodiazepine previously
- clonazepam boluses may be useful

Confusion (see delirium section)

Non-pharmacological management

- look for reversible causes
- aim for minimal disruption and have familiar people in the room

Oral drugs

- haloperidol drops (2 mg/mL - 0.1 mg per drop), initiate at 1 to 2 mg prn and titrate to response (much higher doses may be required - see haloperidol page)
- in frail or elderly patients an initial dose of 0.5 to 1 mg prn may be sufficient

Subcutaneous drugs

- haloperidol by continuous infusion 1 to 10 mg over 24 hours
- boluses of 1 to 2 mg may also be used

Excess secretions (see 'Excessive (retained) secretions' p. 47)

Non-pharmacological management

- consider position change
- it may be distressing to the family/carers rather than the patient

Drugs

- glycopyrrolate 0.6-1.2 mg subcut over 24 hours as a starting dose may help (may increase to 2.4 mg)
- hyoscine (Scopaderm™) patch may be applied behind the ear although confusion and other anticholinergic side effects may occur

- hyoscine butylbromide may be useful 20 mg subcut followed by 30 to 60 mg by continuous subcutaneous infusion over 24 hours
- secretions may become thickened and plugs may form

After death review

It can be helpful for teams to review what happened in order to learn from each patient and family.

- What things went well? What lessons have been learned that can be carried to the next person and family?
- Did the patient and family resolve all unfinished business?
- Were all opportunities to say goodbye taken?
- Was death peaceful and dignified?
- Was everything possible done to care for the family and friends?
- How could care have been improved?
- How does each of the team of professional carers feel?

Palliative chemotherapy

- palliative (i.e. non-curative) active treatments include surgery, chemotherapy and radiotherapy
- monoclonal antibody and immunotherapy drugs are being used more commonly with effect
- signal transduction inhibitors are also being used for longer (such as EGFR, BRAF, BCR-ABL, HER2 and ALK inhibitors)
- two thirds of all chemotherapy treatments given are with 'palliative' intent
- the aim is the palliation of symptoms but the benefit of treatment should exceed the adverse effect on quality of life
- patients of all ages who present late with chemoresponsive tumours may benefit from chemotherapy
- a few patients will gain improved survival while others may get symptom relief or time to prepare for death
- patients need to be carefully supported medically, especially if frail at the time of treatment
- although doctors may be reluctant to give chemotherapy to very ill patients, patients are often keen to try it, even if the benefits may be small

Benefits

- an often only modest survival gain of months
- chemotherapy-induced symptoms are less disruptive to quality of life than the effects of the cancer itself
- may also improve the patient and their family's psychological wellbeing because 'something is being done'
- decreased tumour bulk

Adverse effects

- terminal cancer patients who receive chemotherapy during the last months of their

lives are less likely to die where they wish and are more likely to undergo invasive medical procedures

- patients may express more concern about chemotherapy-induced symptoms than about the ultimate effect of the cancer
- bone marrow failure (anaemia, neutropenia, thrombocytopenia)
- unrealistic hope
- avoidance of 'death talks' and preparations
- nausea/vomiting
- lethargy/fatigue
- mucosistis and loss of taste
- peripheral neuropathies e.g. with vincristine
- alopecia
- diarrhoea
- constipation
- stomatitis

Complementary and alternative medicine

- There is no universally agreed definition of Complementary and Alternative Medicines (CAM) but The World Health Organisation defines it as:
- 'A broad set of health care practices that are not part of a country's own tradition and not integrated into the dominant health care system.' Other terms sometimes used to describe these health care practices include 'natural medicine', 'non-conventional medicine' and 'holistic medicine'.
- Complementary and Alternative Medicines (CAM) are widely used in Australasia
- a drug history should include all medicines including CAMs
- CAMs can sometimes adversely impact on conventional therapies
- CAMs use may be influenced by cultural beliefs and behaviours

Health professionals unfamiliar with CAM therapies that their patients are taking should seek information from a drug information pharmacist.