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Gregory B. Crawford, Katherine A. Hauser, and Wendy I. Jansen

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Palliative care: End of life symptoms

Gregory B Crawford, Katherine A Hauser, Wendy I Jansen

Abstract

Caring for people at the end of their life is an important aspect of palliative care. There are international variations in language. In the United Kingdom and Australia, hospice generally refers to a philosophy of care but also relates to inpatient care, where in USA hospice care is generally community-based. Even the meaning of “end of life” can be confusing. The care of people approaching the end of their life is best provided by a multi-disciplinary team. Caring for people with non-curative cancers is likely to be part of the work of medical and nursing staff in almost all areas of healthcare.

There will be times to seek specialist palliative care medical and nursing assistance or advice but there is an imperative that generalists, including general practitioners or family physicians and oncologists, can provide a palliative approach to care when this is appropriate. For cancer patients and their treating physicians, one particularly challenging issue is if or when disease-modifying therapies should be ceased. Involvement of specialist palliative care and taking a palliative approach to care should be encouraged early, not merely at the end of active disease-modifying therapies. There is evidence that early involvement of palliative care may even have a survival benefit. Patients do expect their doctors to initiate conversations about end of life and these conversations can reduce the use of intensive medical treatment at the end of life. If possible it is best to avoid these discussions when the patient is acutely ill or distressed. It is also important to identify the onset of the terminal phase. The diagnosis of impending death is not always easy but is important to ensure appropriate care is provided.

Symptom control is a significant part of the healthcare interventions provided by a palliative care team. Physical symptoms are generally well recognized and have a considerable prevalence (e.g. lack of energy (73.4%), pain (63.1%), nausea (44.7%), lack of appetite (44.5%), constipation (33.6%), cough (29.4%) and shortness of breath (22.9%)). Psychological symptoms are much more challenging to elicit and more controversy exists about what is normal and what might require intervention. Symptoms such as anxiety and depression may not be as easily acknowledged, diagnosed or treated by patients, carers or healthcare providers.

Keywords

palliative care, end of life, symptoms, pain, delirium, psychosocial care.

Introduction

The World Health Organization defines palliative care as “an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”¹ The word “palliative” is derived from the Latin word *pallium*, which means, “a cloak”.² One important facet of palliative care is the relief of symptoms, that is, the covering or cloaking of symptoms. Caring for people at the end of their life is another important aspect of palliative care. However, there are international variations in language. In the United Kingdom and Australia, hospice generally refers to a philosophy of care but also relates to inpatient care, where in USA hospice care is generally community-based.³ Even the meaning of “end of life” should be clarified. In the United Kingdom ‘approaching the end of life’ is when they are likely to die within the next 12 months. This includes those patients whose death is expected within hours or days; those who have advanced, progressive incurable conditions; those with general frailty and co-existing conditions that mean they are expected to die within 12 months; those at risk of dying from a sudden acute crisis of an existing condition; and those with life-threatening acute conditions caused by sudden catastrophic events.”⁴ In USA ‘end of life’ tends to be related to the hospice admission criteria of six months or less of life expectancy^{3,5} and in Australia is commonly used to refer to the last few days of life when a person is irreversibly dying.⁶ We will discuss the care of people in the last days to weeks of life.

The care of people approaching the end of their life is best provided by a multi-disciplinary team.⁷ This will of course depend on local resources and the patient’s needs. Caring for people with non-curative cancers is likely to be part of the work of medical and nursing staff in almost all areas of healthcare. There will be times to seek specialist palliative care medical and nursing assistance or advice but there is an imperative that generalists, including general practitioners or family physicians and oncologists, can provide a palliative approach to care when this is appropriate.

Ceasing active therapies

For cancer patients and their treating physicians, one particularly challenging issue is if or when disease-modifying therapies should be ceased. To accurately prognosticate for an individual person, and assess the likely risk/benefit ratio of a therapy, and thus advise about further disease-modifying options is a complex task. Decision making should ideally be shared between the doctor and the patient and family, where culturally appropriate. Evidence about benefits and potential burdens of new targeted therapies for individuals with advanced disease may be limited or relatively unknown. Goals of therapy and likely future outcomes are generally discussed at the onset of treatment, but nonetheless when therapeutic options are diminishing and the disease is progressing, many people

may not have “heard” or retained understanding about these issues. Discussions should generally involve patient and family and may occur over several consultations and it is clearly best if a consensus can be reached. There are likely to be specific societal, cultural and religious norms that should be understood or asked of patients and their families, to inform with whom these discussions might occur and when. To have an open discussion about ceasing active therapies may not be easy and can take considerable time. However, this approach is likely to provide patients and their families with the opportunity to understand and plan for the approaching end of their life, rather than following a pathway of chemotherapy until death inevitably intervenes. It is useful to frame such decisions in terms of “no longer prescribing chemotherapy” rather than ceasing treatment, with the associated implication of “giving up”, a sense of abandonment and of ceasing to care.

Specialist palliative care

Involvement of specialist palliative care and taking a palliative approach to care should be encouraged early, not merely at the end of active disease-modifying therapies. There is evidence that early involvement of palliative care may even have a survival benefit.⁸ Specialist palliative care services can provide an important coordinating service when contemplating cessation of chemotherapy. Disease progression is frequently associated with increasing symptoms and deteriorating physical function. Palliative care services provide comprehensive symptom assessment and management, equipment and direct nursing care ideally in the home if preferred, but also in a hospice or palliative care unit, an acute hospital or a residential care facility. Discussions about options or choices and the patient and family’s preferences about where death might occur may also be very useful, despite possibly being difficult to raise.

Prognostication

Patients do expect their doctors to initiate conversations about end of life and these conversations can reduce the use of intensive medical treatment at the end of life.⁹ An important part of decision making is the discussion about likely prognosis and how their disease might unfold. This information may affect decisions about treatment, and may change personal choices and priorities.

If possible it is best to avoid these discussions when the patient is acutely ill or distressed. What the clinician is being asked to perform is the use of population-based statistics to give a likely framework of the future for an individual patient and/or their family. A useful start is the ‘surprise question’ i.e. ‘Would I be surprised if this patient were to die in the next 6 to 12 months?’¹⁰ Another instrument is The Supportive and Palliative Care Indicators Tool.¹¹ This uses general indicators of deteriorating health (e.g. recent unplanned hospital admissions, dependence on others for care) and indicators of other illnesses or co-morbidities including cancer, dementia, kidney disease and is designed to assist in recognizing key points in the clinical trajectory.

In advanced cancer, performance status has prognostic significance.¹² The rate of change in performance is generally correlated with increasing burden of disease and increasing constitutional symptoms, e.g. anorexia, cachexia, fatigue. Scores of the Australian-modified Karnofsky Performance Scale (AKPS)¹³ of less than 40 (out of 100) or an Eastern Cooperative Oncology Group (ECOG) performance status score of 3 (out of 4) correlates to a median survival of around three months for patients with advanced cancer.

Most patients and their families want specific and honest information about their prognosis. This should be delivered with compassion, to help them make decisions and plan for whatever time that might remain. If a person does not wish to discuss prognostic information, this should of course be respected but it may be useful to discuss how the discussion may be helpful for planning and decision-making. There may be cultural or religious reasons why some people and families may prefer not to discuss prognostic information at all, or may want a specific family member rather than the individual to receive such information.

When discussing prognosis, it is best to explore why the question is being asked, consider who is asking, check what information they have been given previously and then provide information about prognosis sensitively in terms of ‘days’, ‘weeks’ or ‘months’ that might be reasonably expected. The uncertainty of the prediction and the potential for unforeseeable events such as thromboembolism and infection should generally also be mentioned. When assessing limited prognosis, it is wise to review patient and family needs and care, e.g. undertake a medication review, discuss goals of care and consider whether referral to specialist palliative care or other community supports might provide benefit.

It is also important to identify the onset of the terminal phase. The diagnosis of impending death is not always easy but is important to ensure appropriate care is provided. Common signs and symptoms include very poor performance status, i.e. usually bed-bound, reduced conscious state, difficulty swallowing, reduced urine output, changes in respiratory pattern and signs of peripheral shutdown with mottled skin and cold extremities.

Symptom control

Symptom control is a significant part of the healthcare interventions provided by a palliative care team. Physical symptoms are generally well recognized and have a considerable prevalence (e.g. lack of energy (73.4%), pain (63.1%), nausea (44.7%), lack of appetite (44.5%), constipation (33.6%), cough (29.4%) and shortness of breath (22.9%)).¹⁴ Psychological symptoms are much more challenging to elicit and more controversy exists about what is normal and what might require

intervention. Symptoms such as anxiety and depression may not be as easily acknowledged, diagnosed or treated by patients, carers or healthcare providers.^{15, 16-20}

Ethical decision-making

The ethical principles of autonomy, beneficence, non-maleficence and justice are useful to guide decisions at the end of life. When ethical dilemmas arise there may not be one correct answer. Despite a patient's needs and desires being central to good healthcare, there are limits to individual autonomy. Healthcare providers need to offer choice when there is truly a choice. There are times when patient and family preference may not be possible, because of disease, limitations to therapeutic options, the terminal nature of the condition, and limited resources of public systems and of families.

The central practice of palliative care is a patient-centered approach to care, attention to symptom control, and open communication about what choices there are for the patient as they approach the end of their life. And although the WHO defines the unit of care as being 'patient and family', the patient's right to autonomy and confidentiality remains.

There is real potential for misunderstanding and conflict when negotiating options for care. Decisions may be clinically quite complex and there may be limited evidence to support clinicians. The principle of autonomy supports patients making their own individual choice. In a clinical situation this means respecting an individual's decision to accept or reject investigations and therapies that might provide some benefit. Further difficulties can arise because of concerns about patient capacity or competence and then who might legitimately be charged with making any decisions about care. Many jurisdictions will have legislation to support care and substitute decision making at the end of life. Common sense should guide discussions in areas where there is less clarity. Clear and honest communication is likely to minimize misunderstandings.

Rationalizing medications and interventions and deprescribing

Best palliative care practice is neither to hasten or postpone death, however as a patient's condition deteriorates, the likely benefits and burden or harm of treatments are likely to change. To raise the possibility of ceasing medications that have been taken for many years, with the expectation of prolonging well-being or avoiding future medical complications, can be emotionally confronting. Medications that are unlikely to provide benefit may include lipid lowering medicines. Equally even anticoagulants for cardiac or thromboembolic events may present potentially greater risk if continued, rather than ceased. The relative risk may be greater with continuing, e.g. a patient who is anticoagulated but is experiencing frequent falls. There is a small but growing body of literature to assist with this decision-making.^{21,22} Defibrillator deactivation should be considered in patients who have one implanted.²³

Symptom management

General principles:

For any new or progressive symptoms near the end of life it is important to consider whether potentially reversible causes are contributing, and whether treatment aimed at reversal is appropriate, considering the patient's prognosis, their goals and the location of care and burden and side-effects of treatment. Many symptoms occurring at the end of life may respond at least in part to non-pharmacological management. Due to an impaired ability to swallow safely and reduced consciousness, non-oral routes for medications are likely to be required. Many end of life care medications can be given subcutaneously (SC), sublingually (SL) or per rectum (PR), if intravenous (IV) access is not available or inappropriate e.g., in the home setting.^{24,25} Continuous subcutaneous infusions (CSCI) or SC syringe drivers may contain a combination of medications aimed at multiple symptoms.

Anticipatory prescribing allows common symptoms to be managed more easily if or when they develop and crises potentially averted, regardless of whether the site of care is hospital, residential aged care facility or in the home. A basic kit of four medications (an opioid, benzodiazepine, antipsychotic and anticholinergic) can be provided for home use, or prescribed in hospital to manage most common symptom issues in the terminal phase.²⁵⁻²⁷ Medications used to manage the terminal phase vary according to local availability and regional guidelines should be consulted.²⁷⁻³¹ Regular review and titration of doses is required to ensure symptoms are adequately managed. For persistent symptoms both a continuous background and as needed (PRN or breakthrough) doses will usually be required. The routine use of end of life care pathways has not been demonstrated to improve the quality of care of dying patients.³²

Education and support of family members regarding what to expect and basic symptom management is necessary both at home and in the hospital or hospice. Family caregivers will often be required to give medications in the home and may be anxious about the potential of these medications to cause harm or to hasten death.

Pain

Assessment of pain requires a thorough clinical history and examination followed by correlation of symptoms with known sites of disease and judicious use of investigations. Validated pain rating scales (e.g. a numerical rating scale, visual analogue scale or faces pain scale) should be used.³³ In the terminal phase, assessment may need to rely on non-verbal indicators e.g. frown, grimace, muscle tension, restlessness, guarding or withdrawal when being touched or moved. Validated scales are available for cognitively impaired people e.g. the Abbey Pain Scale.³⁴ Delirium, anxiety,

psychosocial and existential distress may contribute to a lower pain threshold and complicate pain assessment.³³ New or increasing pain may be due to progressive disease, new bone lesions or complications, general aches and pains from bedrest, skin pressure, urinary retention, constipation and mouth ulcers. Attention to good nursing care, to relief of pressure areas with appropriate mattresses or other pressure relieving devices and to bladder and bowel function are all important to minimize pain.

Many people with cancer will have had pain prior to entering the terminal phase and thus have an established analgesic regimen, usually based on a long acting opioid, either oral or topical patch. Oral pain medications may need to be converted to parenteral (either IV or SC) when patients are no longer able to swallow. This is generally done using opioid equivalency charts.^{28,35,36} Fentanyl patches can remain in situ at end of life and additional opioid needs can be managed as for other patients.³⁷ Most will need additional as required (breakthrough) analgesia. Initially breakthrough doses are typically 5 – 15% of the background dose and are then titrated to effect.³⁸ For those who are opioid-naïve, initially small frequent doses of an appropriate opioid should be prescribed and available ‘as required’ and titrated to effect. Once the 24 hour effective dose is established, a continuous infusion can be commenced either SC or IV.²⁸ Breakthrough doses may still be required and the infusion is then titrated based on use. Proportionate opioid titration does not shorten life even in the final days to weeks.³⁹

Signs of opioid toxicity may include myoclonus, delirium, hyperalgesia and allodynia. Options for management include dose reduction or switching of the opioid.⁴⁰ If this is not appropriate e.g. very short prognosis, toxicity can be managed with benzodiazepines for myoclonus or antipsychotics for delirium. There is no consistent evidence that routine use of parenteral fluids alters symptoms at the end of life, including opioid toxicity.^{41,42} Constipation should be anticipated and a prophylactic aperient prescribed if the patient can swallow.⁴³ In the last days of life, constipation may not be a symptomatic issue. Rectal suppositories may be used if there are signs of discomfort.⁴⁴

Renal impairment can impair the clearance of active metabolites of morphine, hydromorphone and oxycodone which may contribute to toxicity.⁴⁵ Fentanyl, buprenorphine and methadone have no active metabolites thus may be better initial opioids for patients with renal failure.^{43,45} Metabolites may also accumulate with impaired renal function occurring as part of the dying process. Hepatic impairment prolongs the half-life of many opiates (morphine, hydromorphone, oxycodone, methadone) and thus may also contribute to accumulation. Cautious dose titration and consideration of increased dosing intervals is recommended.^{46,47} Fentanyl may be a safer opioid in hepatic failure.⁴⁶ Patients already on an opioid who develop liver failure should be observed for signs of toxicity.

Adjuvant analgesics prescribed for neuropathic pain (e.g. anticonvulsants, antidepressants) are generally continued whilst patients can swallow. Anticonvulsant doses may need to be adjusted if the patient has renal impairment. Non-oral adjuvants include non-steroidal anti-inflammatory drugs (ketorolac IV, diclofenac PR, paracetamol IV or suppository) and dexamethasone (SC or IV), used commonly for pain from bone lesions, tumor compression of nerves or other structures, bowel obstruction or headache from intracranial pressure.⁴⁸⁻⁵⁰ Topical analgesia e.g. lidocaine may be useful for painful wounds. Short course radiotherapy may provide effective analgesia for painful bone and other tumors in appropriate patients.⁴⁰

Gastrointestinal symptoms: Nausea and vomiting, constipation, nutrition and hydration.

Nausea and vomiting are frequent in cancer patients and often multifactorial.⁵¹ These symptoms can be less severe in the last days of life due to reduced oral intake.⁵² Nausea and vomiting may be prominent where there is a bowel obstruction, peritoneal disease, large hepatomegaly or severe constipation. Hypercalcemia may contribute to both nausea and constipation. Constipation is very common due to bedrest, medications, particularly opioids and low fluid intake. Non-pharmacological management of nausea and vomiting includes taking only sips of fluid or ice chips. A nasogastric tube may be required if there is a bowel obstruction and vomiting is not responding to pharmacological measures.

Management of nausea and vomiting also includes management of constipation. This may be administered via the rectum if aperients are unable to be swallowed. First line anti-emetics are usually metoclopramide or haloperidol, both of which may be given SC.^{27,28} Ondansetron is used less often as it is constipating, however it is available in wafer form making administration relatively simple.

Hydration and nutrition

Declining appetite, alertness and poor swallowing cause a natural reduction in fluid and food intake at the end of life. Dry mouth is a common symptom and is generally managed with meticulous mouth care and saliva substitutes. Small amounts of fluid and food should be offered when patients are alert and wish to eat and drink. Artificial hydration does not improve symptoms of dehydration at the end of life and is not associated with a survival benefit.⁴¹ Anecdotally, artificial hydration has the potential to worsen fluid overload, ascites, pulmonary edema and respiratory secretions although evidence is lacking.⁴² Decisions around artificial hydration and nutrition frequently cause family distress, with concerns that the patient is dying of dehydration or starvation. Patients are often less concerned due to lack of appetite and reduced awareness. Pros and cons of artificial hydration should be considered and discussed with the patient and family and if desired a time limited trial of hydration

commenced with negotiated outcome measures. Up to 1 liter of normal saline can be delivered subcutaneously over 24 hours in the absence of IV access.

Artificial nutrition is not recommended for cancer patients in the last days to weeks of life. Both enteral and parenteral nutrition are associated with numerous complications and unlikely to alter prognosis in advanced cancer at the end of life.⁴²

Dyspnea

Dyspnea is a subjective sensation of difficulty breathing. In the last days of life patients may not be able to communicate this sensation. Tachypnea and increased work of breathing in a non-verbal or confused patient may indicate respiratory distress, but does not always correlate with subjective symptoms.⁵³ Dyspnea can cause anxiety which in turn worsens the sensation of breathlessness. Potentially reversible factors include bronchospasm, pleural or pericardial effusion, pulmonary edema, anemia, infection and pulmonary embolism. Treatment options should be based on consideration of goals of care and prognosis. Therapeutic drainage of effusions may provide symptomatic relief but can be burdensome for a dying patient.

Non-pharmacological measures to relieve dyspnea include adopting a seated position, a fan blowing toward the face, opening doors and windows, reassurance, and controlled breathing.^{54,55} Oxygen is only of symptomatic benefit if there is hypoxia.⁵⁶ Opioids are the first line palliative pharmacological management of refractory dyspnea.⁵⁷ If already on an opioid for pain, the dose can be increased by 25-50%^{28,31} and the patient and carer encouraged to use breakthrough opioid medication for dyspnea or pain. If the patient is opioid-naïve the same or slightly lower doses as for pain are usually prescribed.⁵⁸ Benzodiazepines are often used for anxiety secondary to dyspnea. Clinical trials of benzodiazepines for dyspnea have in general been negative, however midazolam has been demonstrated to relieve dyspnea in the last week of life in cancer.^{59,60} Bronchodilators, diuretics, and corticosteroids are generally continued if they are providing therapeutic benefit. Steroids may be useful if there is airway compression or lymphangitis carcinomatosa.⁶¹ Anticholinergics are considered if excessive secretions are contributing to breathlessness. A small study of cancer patients with dyspnea refractory to opioids has demonstrated symptom benefit from both high flow oxygen and BiPAP.⁵³ Patients who were enrolled had poor performance status but greater than one week life expectancy, so this may not be applicable to the terminal phase. If dyspnea is severe and persists despite appropriate doses of opioid and benzodiazepine, palliative sedation may be considered.⁶²

Airway obstruction can present as acute severe distress. If it is not possible to relieve the obstruction by corticosteroids or interventional procedures or radiotherapy (if appropriate), sedation may be required to achieve comfort.

Delirium

Delirium is common at the end of life.⁶³ It presents as fluctuating consciousness, attention and cognition, often accompanied by perceptual abnormalities including hallucinations and agitation. Delirium may be hyperactive or hypoactive, which is more often under-diagnosed.⁶³ Screening for delirium is recommended and brief simple tools can be utilized e.g. Confusion Assessment Method, Nursing Delirium Screening Scale.⁶⁴ Environmental and general care measures are advocated routinely to prevent delirium in the elderly hospitalized population.⁶³

Potentially reversible factors should be sought and treated where appropriate.⁶⁵ These include infection e.g. urinary or respiratory tract infection, hypercalcemia, drug toxicity (opioids, steroids, anticholinergics, anticonvulsants), dehydration, and nicotine, drug or alcohol withdrawal. Delirium may be aggravated by urinary retention, constipation or under-treated pain. Irreversible factors may include progressive disease, Central Nervous System involvement by cancer, organ failure and metabolic abnormalities. Routine parenteral administration of fluids in the terminal phase has not been demonstrated to prevent delirium.⁴²

Non-pharmacological management includes calm reassurance, reducing excessive stimulation, providing vision and hearing aids if indicated, clear environmental cues for day and night, and family education and support. Despite lack of supporting evidence, the standard first line pharmacological management has been either typical (e.g. haloperidol) or atypical antipsychotics (e.g. risperidone, olanzapine, quetiapine).⁶⁵ Haloperidol is the commonest first line medication and can be given orally or SC. Olanzapine is available in a wafer which may make administration easier. A recent randomized controlled trial in palliative care inpatients with mild to moderate delirium and an expected prognosis of greater than seven days found increased agitation and shortened survival in those prescribed regular antipsychotic medications.⁶⁶ This has led to particular caution in prescribing psychoactive medications in this population. However, there is evidence that delirium is distressing for patients and families and unmet symptom distress should be proactively addressed with non-pharmacological interventions including family education and support.⁶⁷ Antipsychotics are probably best reserved for those with severe agitation despite these measures.

Vigilance is required to detect extrapyramidal side effects in those prescribed antipsychotics, e.g. akathisia which may manifest as worsening agitation. Caution should be exercised in patients with a diagnosis of Parkinson's disease as typical antipsychotics may worsen movement disorders. Older highly sedating antipsychotics (e.g. chlorpromazine, levomepromazine) may be considered if agitation is refractory and distressing in patients with a short prognosis.⁶⁸ Benzodiazepines are generally used as rescue medications and have a specific role in management of alcohol withdrawal.

Short-acting benzodiazepines may be preferable e.g. midazolam (SC), lorazepam (oral, SL) to avoid daytime drowsiness and sleep-wake reversal. Nicotine replacement should be considered in cigarette smokers.

Respiratory Secretions

Retained respiratory secretions are common in the last days of life.^{69, 70} Impaired swallow and cough mechanisms and reduced consciousness are likely mechanisms. Audible secretions cause rattling breathing ('death rattle') which is often very distressing for the family. Patients are often unconscious at this stage and are thought to be spared the distress of this symptom.⁶⁹ The onset of audible secretions usually implies a prognosis of less than 48 hours.⁷⁰

Secretions may be difficult to eliminate once established. Non-pharmacological management consists of placing the patient in a semi-prone or head up position, meticulous mouth care, cautious suction if secretions are in the mouth and cessation of parenteral hydration if being administered.⁷¹ The mainstay of pharmacological management is anticholinergic medication, despite limited evidence of effectiveness.^{72, 73} Those that do not cross the blood brain barrier (hyosine butylbromide, glycopyrolate) are used preferentially due to the theoretical lowered risk of precipitating delirium.⁶² There is no evidence of differences in efficacy between the available medications.^{74, 75}

Other symptoms

Hemorrhage

Bleeding issues are not uncommon in advanced cancer. However, catastrophic hemorrhage is a rare but very distressing event.⁴⁴ Patients predisposed to bleeding include those with head and neck cancer, bone marrow failure, liver failure and tumors close to major arteries or those eroding hollow organs or the airway. Cessation of anticoagulants and appropriate correction of coagulopathies (e.g. vitamin K replacement, platelet transfusion) may be considered if clinically appropriate. Malignant wounds may bleed and are frequently managed with topical application of hemostatic dressings or agents such as epinephrine or thromboplastin.⁷⁶ Anti-fibrinolytic medications (e.g. tranexamic acid and aminocaproic acid) may be used for patients with thrombocytopenia, altered coagulation or a bleeding tumor, commonly gastrointestinal or gynecological cancers.⁷⁶ Prescribing must also balance the risk of clotting with any potential benefits. Anti-fibrinolytic medications should be used cautiously in hematuria, due to the risk of clot retention.⁷⁷ Local radiotherapy may also have a hemostatic effect for tumors or malignant wounds. Interventional techniques such as endoscopic injection or arterial embolization may also be considered.

Management of catastrophic hemorrhage includes calm reassurance of the patient and family, application of local pressure, suction and dark towels to conceal and absorb blood. Pharmacological

management includes immediate sedation with high dose benzodiazepine and/or opioids given intravenously or intramuscularly (not SC due to impaired peripheral circulation).⁷⁸

Seizures

Seizures are a common complication in the last days to weeks of life for patients with brain tumors.⁷⁹ Seizure frequency is lower in those with metastatic rather than primary tumors.^{79,80} Other causes of seizures include leptomeningeal carcinomatosis, metabolic abnormalities, organ failure, medications (i.e., may lower seizure threshold), drug interactions and drug withdrawal. Many patients with a primary or secondary brain tumor are taking anti-epileptic drugs at the end of life.⁸¹ If merely prescribed prophylactically at the time of surgery (i.e. no history of seizure) these may be discontinued relatively safely.⁸²

When there is a history of seizures, the risk of recurrent seizure activity needs to be considered when a patient is no longer able to swallow oral medication. Often anti-epileptic medications are replaced by non-oral medications. If IV access is available phenytoin, levetiracetam or sodium valproate may be used. For acute treatment of seizures, benzodiazepines are the recommended first line medication. Midazolam may be administered SC, intranasally or IV and diazepam or lorazepam IV or rectally.⁸³ For seizure prevention in the absence of IV access, a continuous infusion of midazolam SC or clonazepam once or twice daily SC can be prescribed.⁸⁴ For refractory seizures phenobarbital may be used IV, SC or IM.⁸³

Psychosocial care

Emotional distress is common and important to recognize at the end of life. The source of distress may be multifactorial; anticipatory grief, fear of dying, spiritual distress, poorly managed symptoms or fear of worsening symptoms, loss of independence and continence, sense of being a burden on caregivers, concern about family and loved ones, family conflict, or unfinished business which may be psychosocial, financial or legal. It is important to consider that poorly controlled physical symptoms (e.g. pain, dyspnea, delirium) and some medications (e.g. corticosteroids, bronchodilators) may contribute to symptoms of psychological distress. Supportive therapies, including spiritual support, should be offered but participation may be limited due to impaired cognition and fatigue. There is evidence that interventions that concentrate on meaning, hope and stress reduction are effective.⁸⁵ Support for completing unfinished business should be provided where possible.

Depression may be difficult to diagnose at the end of life as many symptoms of depression overlap with those of normal dying (e.g. loss of appetite, poor sleep, loss of energy, poor concentration).⁸⁶ Grief and other forms of emotional distress may complicate evaluation. Symptoms of pervasive hopelessness, loss of interest and pleasure, guilt and suicidal ideation may suggest a diagnosis of

depression.⁸⁷ A single question ‘Are you depressed’ is a useful screening tool.⁸⁸ Collateral history from family members may assist in diagnosis. Management of depression should use a combined approach. Supportive psychotherapeutic interventions may be beneficial unless precluded by lack of energy or cognitive deficits.⁸⁹ Most antidepressants take several weeks to provide a therapeutic benefit.⁹⁰ Prescribing will be influenced by the patient’s anticipated prognosis.⁹¹ Sedating antidepressants, e.g. mirtazapine, trazadone, may help insomnia and improve appetite.⁸⁹ For patients established on antidepressants, these are generally continued until they are unable to be swallowed. Psychostimulants may have some symptomatic benefit for depressed mood, fatigue and poor concentration.⁸⁶

Anxiety is common, either as a pre-existing condition or a new symptom and can in turn exacerbate other symptoms. This may be managed with psychological techniques e.g. controlled breathing, visualization, distraction, and hypnosis. Benzodiazepines are frequently prescribed at end of life, either PRN or regularly for anxiety. These may be given sublingually, rectally or subcutaneously when they cannot be swallowed. Serotonergic antidepressants may be indicated for the treatment of anxiety for those with a longer prognosis (i.e. weeks).⁹²

It is important to acknowledge, respect and support spiritual and cultural beliefs and rituals around dying.⁹³ Spirituality may contribute to a person’s beliefs about their illness and its treatment, their sense of meaning and belief in an after-life.⁹⁴ Cultural beliefs may impact on the role of family in information-sharing and decision-making, as well as preferences for end of life care.^{95,96} Clinicians have an important role in eliciting the impact of spiritual and cultural beliefs on patient care.^{94,95}

Family support is important. Family meetings have a role for providing information and support to caregivers, managing family discord, navigating substitute decision making and planning future goals and location of care. Ideally these should be a formalized multidisciplinary meeting following a recommended agenda or framework.^{97,98} Usually the patient will participate unless they have impaired decision making capacity, choose not to, or are unable to contribute due to the severity of their illness.⁹⁹ Caregivers may need support with issues such as caregiving burden, psychological distress, grief, and practical, financial and legal matters.

Requests for hastened death

Requests for hastened death may be a sign of existential or global distress, uncontrolled symptoms, depression or hopelessness or a sense of being a burden. These requests may fluctuate over time.¹⁰⁰ Clinician’s responses should focus on exploring underlying reasons for the request and a supportive response to these concerns.¹⁰¹ A request for hastened death may represent a need to exercise control over the circumstances of dying.¹⁰⁰ In jurisdictions where physician assisted dying is legal, it is an

uncommon cause of cancer death and many who request assisted dying do not eventually use this method.^{100, 102}

Palliative Sedation

Palliative sedation is deep continuous sedation prescribed for patients with very short life expectancy with refractory symptom distress when all other symptom control measures have been exhausted or considered inappropriate. A palliative care consultation should be considered to ensure symptoms are indeed refractory to therapy and for advice on prescription and monitoring of sedation.¹⁰³

Caring at home

For most people with an ultimately terminal cancer, the vast majority of time is spent at home. Some people may have a clear choice about where they wish to be as death approaches.¹⁰⁴ A decision to die at home generally needs to be an active one, with support from family and friends, family doctor and community nursing teams as a minimum. Some people will want and be able to engage in such discussion, and others will not. Many aspire to a home death, but death at home is not necessarily the best death.^{105, 106}

Managing the care of someone at home has specific challenges that are different from inpatient care or clinic management. Clinicians will still need to assess patient needs and access to supports will vary between countries and within regions. As disease progresses, most people will experience some decline in physical function. There is generally a need for simple equipment such as a commode chair, a walking frame and possibly something to raise the toilet seat. Hand rails may improve mobility and safety as well. Mattress protectors and measures to increase comfort and even a hospital-type bed may be available and desired. Many would prefer to remain in their own bed but sometimes a compromise between personal choice and ease of nursing care may require negotiation. It is important to know how to access any publicly funded equipment sources as well as how to hire or purchase other aids that may be of assistance. For some people and their families the best choice may be anticipating death in a Residential Aged Care Facility or Nursing Home, acute hospital or a purpose-built palliative care/hospice facility. Symptom issues, carer fatigue or carer illness or a change of mind may result in a changed site of care and ultimately site of death.^{107, 108} Systems should be responsive to ensure that such changes in location of care are as seamless as possible.

To manage at home, most people will require the support of a personal carer or family member. As the disease progresses and function deteriorates this need may become almost constant supervision. Between jurisdictions there will be varying access to nursing care in the home and other respite options. Nevertheless, a significant burden of personal care will generally fall to family caregivers.

Research has identified that access to assessment and support from healthcare professionals is vital.¹⁰⁹ Many carers are fearful about deterioration and knowing whether an intervention is required or not.¹¹⁰ They report a lack of skills to assess and manage symptoms. Concern about medication management is frequent.¹¹¹ Other family members may add to the burden, perhaps inadvertently and carers may find that they have little or no time to perform other tasks for themselves. There is a significant risk to the health of a person who is caring.¹¹² Both they and the patient are likely to need significant psychological support as well as physical support.

As death approaches and patients are increasingly frail, particular attention will need to be paid to skin care. Simple measures such as clean, taut sheets and measures to minimize moisture or soiling from urinary or fecal incontinence are important. Mattress underlays and incontinence pads and other devices assist. Attention to mouth hygiene, clean teeth and hydration of lips and tongue is important. Infections such as candida and herpes can reduce quality of life significantly. There are various proprietary preparations to moderate many of these symptoms.

In summary, it is important to ensure that every person who is approaching the end of their lives from cancer is provided with a patient-centered focus to care, has responsive assessment of their needs and there is attention to physical, emotional, psychological and spiritual aspects of care using therapeutic communication skills, and a collaborative approach by a clinical team.

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