Emergencies in Palliative Care

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Abstract: Palliative care emergencies are emergencies in patients with an incurable disease that may lead to death or decreased quality of life. During the palliative care phase of a patient’s life, they differ from other medical emergencies and are mainly focused on symptom control, whereas disease-oriented treatments are less important. Palliative care emergencies can occur on the physical, emotional, and existential field. They involve not only the patient but also the family and sometimes the health care professional. Palliative care emergencies that are addressed are pain, acute dyspnea, major bleeding, acute function loss, acute anxiety, delirium, epileptic seizures, acute decompensation with aggressive behavior of the nonprofessional caregiver, and planning for predictable emergencies.

Key Words: Palliative care emergencies, physical, emotional, existential, decompensation, acute function loss, pain

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Medical emergencies are situations and/or conditions during which the life and the quality of life (QoL) of a patient is threatened and, if no intervention is done, can lead to the death of the patient or a decrease in QoL. Several kinds of medical emergencies have been identified and are discussed according to the disease system (eg, oncological emergencies, cardiac emergencies) or according to the discipline (eg, surgical emergencies, radiotherapeutic emergencies). They have been discussed in reviews on the approach and treatment, and they are not the scope of this review.

Palliative care, defined according to the World Health Organization, provides relief from pain and other distressing symptoms; affirms life and regards dying as a normal process; intends neither to hasten or postpone death; integrates the psychological and spiritual aspects of patient care; offers a support system to help patients live as actively as possible until death; offers a support system to help the family cope during the patients’ illness and in their own bereavement; uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated; enhances QoL; and may also positively influence the course of illness. It is applicable early in the course of illness in patients with incurable disease in conjunction with other therapies that are intended to prolong life and includes those interventions needed to better understand and manage distressing clinical complications.

Although palliative care should be implemented early in patients with incurable disease, emergencies specific to palliative care or end-of-life care should focus mainly on QoL; otherwise, the emergency can be regarded as a disease-specific emergency such as spinal cord compression, or metabolic emergencies are regarded as oncological emergencies.

Palliative care emergencies thus focus mainly on QoL and evaluate the physical, psychosocial, and existential impact of the emergency on the patient and the family. Although there are data on emergencies in specific conditions, research on emergencies in palliative care or end-of-life patients is limited, and data are scarce. This review therefore discusses specific complaints that are thought to impair QoL in palliative care setting without focusing on disease-specific emergencies.

PAIN

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Uncontrolled pain should be regarded as an emergency in the palliative care patient because it has a profound impact on QoL.

Pain is often present in the palliative care phase. In cancer patients, its occurrence depends on the type of tumor: it is high in patients with head and neck cancer and genitourinary cancer, whereas it is less frequently observed in patients with hematologic malignancies. In elderly patients with dehilities, it can be observed in more than 50% of patients.

Many patients with otherwise controlled chronic pain experience episodes of acute exacerbation of short duration (up to 60 minutes) (= breakthrough pain). In cancer patients, its prevalence ranges between 65% and 85%. In noncancer patients, its prevalence is similar, and approximately 74% of them are experiencing severe to excruciating breakthrough pain.

Characteristics of Pain

Pain has different characteristics based on a temporal relationship to the pain stimulus or pathophysiological mechanism.

Temporal Relationship

Most patients in the palliative care setting have chronic pain, whereas acute pain can occur because of medical interventions (eg, punctures) or disease progression and complications (eg, pathological bone fracture).

Breakthrough pain in patients with controlled chronic pain should be evaluated because different types of breakthrough pain can be present:
- Idiopathic (or spontaneous) pain, which occurs without warning and has no precipitating cause.
- Incident pain, which has an identifiable cause. It can be voluntary such as initiation of a movement or involuntary such as visceral pain when eating.
- End-of-dose failure, which results when the dose of drug drops below the analgesic level.

Pathophysiological Mechanism

Pain can also be classified based on the pathophysiological mechanism as nociceptive, neuropathic, or mixed pain.

Nociceptive pain is linked to receptor activation by different stimuli, which are transmitted by specific sensory nerves to the sensory cortex. They also stimulate and are modulated by different areas of the brain involved in other processes such as emotion, anxiety, or defense mechanisms.
Neuropathic pain is due to nerve injury and leads to modification of the nerve itself, making it more sensitive to stimuli or inducing a permanent stimulation of higher nerves.

**Diagnosis**

Diagnosis and differentiation of pain are made by anamnesis, and specific instruments can be used to differentiate between nociceptive and neuropathic pain (eg, DN4 questionnaire).

**Treatment**

Treatment depends on the type and pathophysiological mechanism and can be etiologic and/or symptomatic. The acute symptomatic treatment of pain is mainly by analgesics or coanalgesics.

**Acute Nociceptive Pain**

Chronic nociceptive pain can be treated symptomatically with analgesics according to the World Health Organization Pain Ladder. Patients with mild pain are treated with nonopioids such as paracetamol or nonsteroidal anti-inflammatory drugs, and those with moderate to severe pain with fast-acting opioids. Once the medication is started, it should be given in a continuous way (by the clock) to prevent and control pain in the easiest administration form (oral, rectal, transcutaneous after a titration period) and adapted to the individual patient.

Adjuvant analgesics or coanalgesics can be added to better control acute pain (Table 1).

**Acute Neuropathic Pain**

Acute neuropathic pain can be treated with analgesics, although sometimes this leads to suboptimal controlled pain. Other drugs that can be used are antiepileptics, antidepressants, and local anesthetics, but they need a certain build-up period to be effective.

**Breakthrough Pain**

Breakthrough pain should be prevented if possible, or treated immediately. With the development of fast-acting opioids with short duration, this type of pain can be effectively controlled in most patients. The most used agent is fentanyl, and different forms (lozenge, oral patch, sublingual, intranasal) are becoming available.

In patients at the end of life, pain can remain a problem. The administration of medication to control pain becomes a problem because of difficulties of swallowing or decreased systemic circulation causing a change in dermal absorption. In these patients, a parenteral administration (s.c., i.v.) of opioids may be indicated to control chronic pain (continuous administration) or breakthrough pain (as needed).

**Acute Pain Crisis**

Cancer patients can experience an acute increase in pain because of an acute event (eg, pathological fracture, vascular obstruction), resulting in an acute pain crisis. Pain should be controlled by parenteral opioids at a dose calculated according to prior opioid use. For opioid-naive patients, the dose should be morphine 5 to 10 mg s.c. or i.v. For patients previously on opioids, the dose should be approximately equivalent to 10% of total daily dose in parenteral equivalents (ie, for patient on controlled release morphine tablets 200 mg twice a day; this is equivalent to 120 to 150 mg parenteral; therefore, the initial parenteral dose should be 15–20 mg). Pain should be reassessed after 20 minutes, and the dose can be repeated in case of inadequate relief as long as the patient is not excessively sedated.

This process can be repeated either until pain relief is achieved or until the patient starts to demonstrate dose-limiting adverse effects such as excessive drowsiness or myoclonus.

If the pain is due to either bone metastases or compression of neural structures, one can also consider a trial of high-dose steroids, that is, dexamethasone 40 to 100 mg. If this helps, that dose can be gradually tapered while the underlying cause of the pain is being addressed.

If the pain does not respond to aggressive administration of analgesic pharmacotherapy and the patient is very distressed, sedation using parenteral midazolam can be considered as an option of last resort in dying patients (see Refractory Symptoms and Palliative Sedation). In such cases, it is recommended to seek the input of a clinician with specific expertise in the management of cancer pain.

**TABLE 1. Emergency Medication in Palliative Care Setting**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
<th>Dosing Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>Muscle spasm/myoclonus</td>
<td>2–10 mg every 6–8 h (p.o.)</td>
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<tr>
<td></td>
<td>Delirium</td>
<td></td>
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<tr>
<td></td>
<td>Dyspnea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>Midazolam</td>
<td>Muscle spasm</td>
<td>0.3–0.5 mg/kg (s.c.)</td>
</tr>
<tr>
<td></td>
<td>Epileptic insult</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Palliative sedation</td>
<td>Start 5 mg then 1–7 mg/h (s.c.)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Edema, inflammation</td>
<td>8–16 mg every 24 h (p.o., i.v.)</td>
</tr>
<tr>
<td></td>
<td>Nerve compression</td>
<td></td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Delirium</td>
<td>5 mg every 1 h up to 30 mg every 24 h</td>
</tr>
<tr>
<td>Opioids</td>
<td>Pain</td>
<td>10 mg every 6–8 h (p.o.)</td>
</tr>
<tr>
<td></td>
<td>Dyspnea</td>
<td>5 mg every 6–8 h (s.c.)</td>
</tr>
<tr>
<td>Spasmolytics</td>
<td>Visceral spasm</td>
<td>5 mg (s.c.)</td>
</tr>
<tr>
<td>Butylhyoscine</td>
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</table>

**ACUTE DYSPNEA**

Dyspnea is defined as an uncomfortable awareness of breathing and is a common symptom in palliative care patients. Acute dyspnea is the most frequent reason for an emergency admission in palliative care and impacts severely the QoL.

The main causes for acute dyspnea are cardiovascular problems (eg, pulmonary edema, pulmonary embolism), pulmonary problems (eg, bronchial occlusion by tumor or pleural effusion with atelectasis and shunt), acute anemia, or psychological distress.

**Diagnosis**

Because acute dyspnea is a subjective complaint, the patient can only determine the severity of dyspnea. Acute dyspnea can be associated with tachypnea and the use of accessory respiratory muscles. Other symptoms can be pallor, cyanosis, or tachycardia. Patients with large airway obstruction can show inspiratory stridor.
On clinical examination, one can determine the presence of pleural effusions and cardiac failure with increased central venous pressure or edema. The arterial oxygen concentration does not correlate with the severity of the dyspnea, but can indicate the presence of hyperventilation or hypoxia (eg, pulmonary embolism).

Other diagnostic tests that can be useful are the determination of hemoglobin level (acute anemia) and D-dimers (pulmonary embolism). A chest x-ray radiograph can show the presence of infiltrates, atelectasis, or pleural effusions.

Treatment

Etiological Treatment

Patients with a specific diagnosis will benefit from a specific treatment: use of anticoagulation for pulmonary embolism, opiates and diuretics for pulmonary cardiovascular edema, antibiotics in the case of pneumonia, or blood transfusions in the case of anemia.

Radiotherapy or interventional procedures such as using laser and stenting can be used in case of large airway obstruction.

Symptomatic Treatment

Acute dyspnea can be symptomatically treated with oxygen and medication.

- Oxygen is indicated in patients with hypoxia. In patients without hypoxia, its effect has not been proven.
- Systemic opioids are the treatment of choice for the symptomatic control of acute dyspnea.9 Several randomized controlled trials in cancer and noncancer patients have shown a beneficial effect of systemic opioids for acute dyspnea. In opioid-naïve patients, 5 mg s.c. morphine sulfate is effective, whereas for patients receiving baseline opioids, a 25% increase in the baseline dose may provide relief of acute dyspnea. Nebulized opioids are not indicated for the treatment of acute dyspnea.
- Benzodiazepines can be used for acute dyspnea, but in randomized trials, their benefit seems limited for this indication. In patients with anxiety disorders or in case of palliative sedation for refractory acute dyspnea, they can be used.
- Bronchodilators and corticosteroids can be used in case of a reversible airway obstruction.

MAJOR BLEEDING

Major bleeding is an emergency situation in palliative care. It causes distress to the patient and also to the family and the professional health caregiver. Major bleeding may be caused by disorders of the blood vessels, qualitative or quantitative platelet abnormalities, or coagulation disorders.

In patients with advanced hematologic malignancies, major bleeding was reported in up to 30% of patients.10 In patients with solid tumors, bleeding depends on the type and location of the tumor (eg, high in cervical cancer and bronchial cancer).1

Patients may present with visible or internal bleeding. They can show signs of hemodynamic instability (eg, tachycardia, orthostatic hypotension, syncope, shock).

Diagnosis

Diagnosis is based on clinical findings (eg, visible blood loss), and the place of an internal bleeding might be shown by endoscopy (eg, gastric bleeding) or selective angiography. Other signs are anemia and reticulocytosis, thrombocytopenia, and prolonged prothrombin time with an international normalized ratio of more than 1.5.

Prevention

In patients with a hematologic malignancy, bleeding due to thrombocytopenia can be prevented by keeping the blood platelet count to greater than 10 × 10^9/L.

Treatment

Treatment depends on the advanced directives that are discussed with the patient. If there is a “do not resuscitate” directive, comfort measures (eg, sedation) should be taken.

In all other situations of major bleeding and if indicated, hemodynamic stabilization with transfusions and volume repletion should be given. The patient should be admitted to an intensive care unit for resuscitation and close observation.1

Patients with active bleeding and a coagulopathy or low platelet count (<50 × 10^9/L) should be transfused with fresh frozen plasma or blood platelets, respectively. In case of a visible external bleeding, local pressure may be used to control the bleeding; internal bleeding can be controlled by endoscopic hemostatic therapy or angiographic embolization. In patients with bleeding tumors (eg, cervical cancer, endobronchial tumor), hemostatic external beam radiotherapy or brachytherapy can be applied to stop the bleeding. Symptomatic treatment of low-grade bleeding can be by tranexamic acid (10 mg/kg per dose i.v. at 3–4 times per day).1

In case of major bleeding that occurs at the end of life, palliative sedation is indicated for comfort reasons. However, a major bleeding can result in death within minutes. It is of importance that in that case there is adequate care for the family and exposed caregivers.

ACUTE FUNCTION LOSS

The acute loss of a function can constitute an emergency in palliative care patients. Acute loss of a voluntary (eg, motor function such as pareses or paralyses of legs) or involuntary (eg, fecal or urinary incontinence, urinary retention) function impairs the QoL. Importantly, immediate diagnosis and treatment are necessary for recovery of functionality.

Acute Motor Loss

Causes

The cause of acute motor function loss can be local (eg, pathological fracture) but is most commonly due to a lesion in the nervous system (eg, spinal cord compression; nerve compression, brain metastasis, leptomeningeal carcinomatosis).1

Diagnosis

Pathological Fracture of Long Bones

Patients with a pathological fracture present with moderate to severe pain that is worsened by movement. There may be swelling and subcutaneous bleeding at the place of the fracture. Gross deformities can occur in case of associated dislocation. There might be tenderness over the fractured bone.

Diagnosis is made by radiography of the painful region.

Spinal Cord Compression

Spinal cord compression may be due to a fracture of a vertebra, tumor invasion of the spinal canal, or meningeal disease. It occurs in 5% to 10% of cancer patients.

Neurologic signs of spinal cord compression may be patchy and atypical; however, there should be a high index of suspicion in patients with known vertebral metastases, who experience progression of back or radicular pain, or any progressive gait difficulties. Sphincter symptoms such as urinary retention may be a late feature.
The diagnosis of spinal cord compression is made by magnetic resonance imaging (MRI) of the spinal axis.

Peripheral Nerve Compression
Peripheral nerve compression is a process that may take some time and is seen in patients with lymph node metastases or visceral metastases close to large nerves (eg, sciatic nerve). Patients first complain of sensory deficits, but when the disease progresses, functional loss may occur.
Diagnosis is made by electromyography and computed tomography scan or MRI.

Brain Tissue Compression
Patients with brain tissue compression (brain metastases, bleeding) may complain of headache, vomiting, or visual disturbances. The functional loss is typically hemispheric and may be accompanied by epileptic insults.
Diagnosis is made by computed tomography scan or MRI of the brain.

Leptomeningeal Carcinomatosis
Leptomeningeal carcinomatosis presents with clinical manifestations in the neurologic function of the cerebral hemispheres (15%), the cranial nerves (35%), and the spinal cord and roots (60%). Diplopia is the most common symptom of cranial nerve dysfunction, whereas involvement of the spinal cord regions may result in weakness of the extremities.
Diagnosis is made using MRI and cerebrospinal fluid cytology.

Prevention
Because acute motor function loss has such an impact on the QoL of the patient, prevention should be aimed at the occurrence of a fracture. A high level of suspicion in cancer patients should be present in case of known bone metastases and pain.
In patients with an osteolytic lesion involving more than 50% of the cortex of a long bone, a preventive orthopedic intervention is indicated.
In case of metastatic disease in a vertebral body with involvement of the posterior wall, preventive radiotherapy may be given to the affected region.

Treatment
The treatment of acute motor function loss depends on the disease status of the patient. If the expected survival of the patient is still several months, an etiologic treatment can be given. In case of a short life expectancy, only symptomatic treatment is indicated, with control of pain as the principal aim.

Pathological Fracture of Long Bones
Initial management of a pathological fracture of a long bone is immobilization by a splint of fixation and pain treatment.
Traction may be used to reduce the patients’ discomfort and is indicated for immobilization in case of signs of neurovascular compromise.
Definite treatment is by an intramedullary nail followed by radiotherapy. In patients at the end of life, fixation and traction might be an option to alleviate pain. However, this immobilizes the patient.

Spinal Cord Compression
Patients with a diagnosis of spinal cord compression should be nursed flat with neutral spine alignment until bony and neurologic stability is ensured.

All patients with a diagnosis of spinal cord compression in palliative care should receive a loading dose of corticosteroids (eg, 16 mg dexamethasone). Corticosteroids should be continued until treatment with emergency surgery or radiotherapy.
The blood glucose levels should be monitored during corticosteroid treatment. Definite therapy is by neurosurgical decompression followed by radiotherapy in case of motor deficit; in case of sensory deficit, radiotherapy can constitute definitive treatment.

Peripheral Nerve Compression
Acute peripheral nerve compression should be treated with anti-inflammatory drugs. In selected patients, surgery or radiotherapy can be used for decompression.

Brain Tissue Compression
In patients with symptomatic brain metastases, corticosteroids can control peritumoral edema. If the symptoms of motor deficit improve, whole-brain irradiation can stabilize the situation. If there is no improvement with corticosteroids, radiotherapy is effective, but its beneficial effect is difficult to predict.

Leptomeningeal Carcinomatosis
Prognosis of leptomeningeal carcinomatosis is dismal. In patients with a symptomatic hydrocephalus, a ventriculoperitoneal shunt can be placed; radiotherapy can be used to palliate symptoms due to a cauda equina syndrome or cerebrospinal fluid flow disturbances due to localized obstruction; and intrathecal chemotherapy (eg, methotrexate, cytarabine, thiotepa) should be used in chemotherapy-sensitive cancers.

Acute Urinary Retention
Acute urinary retention is a common problem in palliative care patients. Acute urinary retention can be caused by outflow obstruction or neurologic impairment. Neurologic impairment leads to dysfunction of the urinary sphincter and inefficient detrusor muscle contraction resulting in overdistention of the bladder.
Besides prostate enlargement in men (eg, benign prostate hypertrophy, prostate cancer), other causes of acute urinary retention are medication use (eg, opioids), constipation with fecal impaction, neurologic disease, infection, obstruction due to tumor, or psychological issues.
Patients complain of the inability to pass urine and of lower abdominal or suprapubic discomfort. They may become restless or confused. It there is an acute component complicating a chronic obstruction, these symptoms may be less pronounced. In this case, the patient can complain of urinary incontinence and can develop acute renal failure.
Diagnosis is made by clinical examination.
Patients with an acute urinary retention are treated with bladder decompression by urethral or suprapubic catheterization. Partial drainage and clamping are not necessary and may increase risk for urinary tract infection.
Relief of urinary tract obstruction can lead to an increased urine production with excretion of excess fluid retained during the period of obstruction. In patients with renal failure, it can worsen renal function, and compensation with intravenously administered saline may be indicated in selected patients.

Acute Bowel Obstruction
Acute bowel obstruction is the result of interruption of the normal intestinal flow. It can be caused by intraluminal or extraluminal processes (eg, tumor, metastatic disease, strictures)
or due to functional impairment of the gastrointestinal tract (eg, medication use, carcinomatosis).

The most common symptoms of bowel obstruction are abdominal distention, vomiting, abdominal cramps and pain, and the inability to pass flatus. In proximal obstruction, nausea and vomiting are more prominent compared with distal obstruction. Abdominal pain is frequently described as periumbilical and crampy, with paroxysmal episodes of pain occurring every 4 to 5 minutes.1

Diagnosis is made by clinical examination with high-pitched or hypoactive bowel sounds and a plain abdominal radiography with air and fluid-filled loops.

The etiological treatment of malignant bowel obstruction can be a surgical intervention to relieve or bypass the obstruction. However, in palliative care setting, this treatment approach is limited to carefully selected patients with an excellent performance status. Most patients are not candidates for surgery. The placement of a stent through the obstructive part can be considered in selected patients.

The symptomatic treatment is by placement of a nasogastric tube and intravenously administered fluids. A nasogastric tube relieves effectively nausea and vomiting. In case of subobstruction, corticosteroids may solve the obstruction. Octreotide, a somatostatin analog, can alleviate vomiting and even permit removal of a nasogastric tube in patients with terminal cancer and malignant bowel obstruction by reducing gastrointestinal secretion.13

**ACUTE ANXIETY**

Acute anxiety is a state of worry and fear resulting from the perception of a current or future threat to oneself. It is a common symptom in patients facing life-threatening illnesses. At least 25% of cancer patients and 50% of patients with chronic heart failure and chronic obstructive pulmonary disease experience significant anxiety. At least 3% of patients with advanced cancer and 10% with chronic obstructive pulmonary disease meet Diagnostic and Statistical Manual of Mental Disorders criteria for generalized anxiety disorder.14

Anxiety may be present as part of one of several psychiatric disorders, medication use (eg, corticosteroids), withdrawal (eg, alcohol, benzodiazepines), or metabolic reasons (eg, hyperthyroidism).

During the palliative care phase, it is often associated with physical symptoms such as pain, dyspnea, cardiac disturbances, or psychological and existential distress.

Diagnosis is made by anamnesis, which should focus on prior episodes of anxiety, depression, and alcohol and drug use. Physical symptoms of anxiety are sweating, dyspnea, muscle tension, tremulousness, and tachycardia.

Acute treatment is by benzodiazepines (eg, clonazepam 0.25–0.5 mg every 12 hours or lorazepam 0.5–1.0 mg every 8 hours orally). In patients who cannot swallow, midazolam (5 mg) can be administered subcutaneously.

After the acute episode, cognitive behavioral therapy has been shown to decrease anxiety, depression, and worry.

**DELIRIUM**

Delirium is an acute confusional state and is present in up to 85% of palliative care patients at the end of life. It is a distressing condition for patients and their families and is a frequent cause of hospital admission at the end of life.15

The cardinal features of delirium are a fluctuating mental state, disorganized thinking, and an abnormal state of arousal, either hyperactive and agitated or hypoactive and passive. It can have an acute onset.

In palliative care patients, delirium is frequently multifactorial, and some of these can be reversible. Medication is an important cause of delirium at the end of life, and decreasing or stopping medication may be helpful to alleviate the condition. Other causes are withdrawal, infections, metabolic disturbances (eg, hypercalcemia), or hypoxia.

Delirium can be apparent but is not diagnosed by the professional health caregiver in approximately 22% to 50% of patients. To detect changes in mental state due to delirium, the Mini-Mental State Examination can be used as a screening tool for cognitive impairment. The Memorial Delirium Assessment Scale has been validated in patients with advanced cancer, whereas the Delirium Rating Scale has been used to monitor delirium in patients with terminal disease.

The treatment aim of delirium is to calm the patient and help recover his/her ability to communicate. In approximately 50% of palliative care patients, delirium can be reversed by appropriate measures.

Etiological factors should be excluded and treated if possible.
- The medication list of the patient should be evaluated, and medication that can cause delirium should be stopped. If opioids are suspected, opioid rotation might be tried. Metabolites of medication can be decreased by adequate oral or parenteral hydration.
- Metabolic disturbances such as hypercalcemia, hyponatremia, and hypoglycemia should be treated.
- Hypoxia can be treated with oxygen.
- Infections can be treated with antibiotics.

Symptomatic measures can ameliorate or relieve delirium if started immediately.

**General Approach**

- In the first stages of delirium, the patient may be aware of the mental alterations, and at this moment, it is important to reassure him/her.
- The patient should be stimulated to perform easy tasks, such as eating, but excessive demands should not be made, because emotional stability is weakened.
- The patient should be approached in an empathic and respectful way.
- The environment should be safe, comfortable, and relaxing and should be familiar to the patient.
- The family should be explained that the patient is not “losing his/her mind,” that it may not necessarily be accompanied by pain or severe suffering, and that the delirium can fluctuate throughout the day.

**Drug Treatment**

In case a patient becomes agitated or has perceptual disturbances (eg, hallucinations, nightmares), symptomatic drug treatment is indicated.

**Neuroleptics.** Haloperidol is effective in both hyperactive and hypoactive delirium and is the treatment of choice. It can be administered orally, subcutaneously, intravenously, or intramuscularly. The initial dose is 2.0 mg p.o. or 1.0 mg s.c. every 6 hours, with an additional dose every hour if needed. Haloperidol has few such adverse effects as extrapyramidal symptoms with muscle stiffness, dyskinesia, and trembling.

In case of agitated delirium, more sedative neuroleptics such as levomepromazine or chlorpromazine can be used.

Low doses of risperidone (0.5–1.0 mg every 12 hours) can be used in patients with brain tumor-induced behavioral
disorders, in organic brain syndromes, and in elderly patients. Olanzapine (5–12 mg every 24 hours) may be useful in advanced cancer delirium because of its strength, its scarce pharmacological interactions, and its broad therapeutic range.

**Benzo diazepines.** Benzo diazepines are effective in delirium associated with convulsions or in those induced by alcohol or sedative withdrawal. Also, if a delirium does not respond to haloperidol or in case of severe agitation, a trial with benzodiazepines (eg, lorazepam 0.5–1.0 mg every 1–2 hours) is recommended. However, when used as single agent, benzodiazepines might not control delirium and worsen confusion and cognitive disturbance.

When sedation is indicated, midazolam has a rapid effect. It is administered in an initial s.c. dose of 3 to 5 mg that can be repeated every 6 hours or in a continuous subcutaneous administration (30–60 mg every 24 hours).

**Terminal Agitation**

Terminal agitation is a delirium at the end of life. The patient is agitated, has an impaired consciousness, and can show distressed vocalizing, muscle twitching, myoclonus, or convulsions. This situation is very distressing for the family and the professional caregiver.

This kind of agitation can be treated in a similar way as a delirium. If no response is obtained by neuroleptics, a palliative sedation should be started.

**EPILEPTIC SEIZURES**

Epileptic seizures result from electrical hypersynchronization of neuronal networks in the cerebral cortex. Different types of epileptic insults are recognized ranging from simple partial seizures (auras) to generalized seizures with absence seizures (petit mal) to tonic-clonic seizures (grand mal).

During palliative care, it can occur in patients with brain metastases, primary brain tumors, cerebrovascular accidents, or metabolic disorders (eg, hyperglycemia, hypercalcemia or hypocalcemia, hyponatremia) or can be due to medication or substance withdrawal (eg, alcohol, benzodiazepines).

Diagnosis is made by (hetero)anamnnesis, clinical picture, and electroencephalography.

The initial treatment of a patient with an acute epileptic seizure is to ensure his/her safety and adequate oxygenation by ensuring an open airway (eg, removing vomit, insertion of an oral tube).

Thereafter, if possible, intravenously administered diazepam should be administered and can control acute seizures in more than 80% of patients. Rectal administration is an alternative if the intravenous route is not possible. Buccal or intranasal midazolam is another possible treatment. Also, subcutaneously midazolam (5 mg) can be used to control acute seizures, although the literature on this method of use is very limited.

In patients with a status epilepticus refractory to benzodiazepines, phenytoin or phenobarbitone might be used to control the seizures.

**REFRACTORY SYMPTOMS AND PALLIATIVE SEDATION**

Refractory symptoms are symptoms that cannot be adequately controlled despite every tolerable effort to provide relief within an acceptable time period and without compromising consciousness. Dyspnea and delirium are among the most common refractory symptoms in palliative care patients.16

The treatment of refractory symptoms is by palliative sedation, which is defined as the process of the intentional administration of sedative drugs in dosages and in combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms. This procedure should be discussed in advance with the patient and the family.

The sedation is performed by continuous administration of benzodiazepines (eg, midazolam loading dose of 5 mg s.c. followed by a continuous s.c. infusion of 1 to 7 mg/h) or by anesthetic drugs (eg, propofol 0.3–0.4 mg/kg per hour in continuous i.v. infusion). Pain medication is continued, and a bladder catheter is placed. Prevention of complications (eg, pressure sores, corneal ulceration) is intensified, and the support for the family is expanded. The median duration of a palliative sedation is between 1 and 5 days, but it does not hasten death.17

**ACUTE DECOMPENSATION WITH AGGRESSIVE BEHAVIOR OF THE NONPROFESSIONAL CAREGIVER**

Many nonprofessional caregivers experience profound feelings during the palliative care and end-of-life care phase. Emotions can range from love, comprehension, support, satisfaction, denial, sadness, anxiety, and (anticipated) grieving, to overt aggression. During the last phase of life of a patient, many nonprofessional caregivers are under a constant stress that can lead to acute decompensation with aggressive behavior.

Acute decompensation can lead to dangerous situations, not only for the person himself/herself, but also for the immediate surroundings and the professional health caregiver.

Several factors should be taken into consideration when this occurs such as previous reactions to stressful situations, known coping mechanisms, and presence or absence of (familial) support.

Prevention of decompensation of nonprofessional caregivers should be initiated when palliative care is started for a patient: support of the family members on psychological and social issues, agreement on how to deal with burden at the end of life (time table for attending to the dying person), evaluating and strengthening the social network of the caregiver, and encouraging communication between the nonprofessional and professional caregiver.

Acute decompensation of the nonprofessional caregiver often leads to the hospitalization of the patient, to aggressive and destructive behavior to his/her family members or professional caregiver, or to self-inflicted harm.18

If a nonprofessional caregiver becomes aggressive, several measures should be taken to avoid harm:

- The person is led to a private but not isolated area while keeping in mind that he/she is not blocking the escape route.
- More than 1 professional caregiver should be involved in the interaction.
- Persons who are agitated but cooperative may be amenable to verbal de-escalation techniques. Actively violent persons and uncooperative, agitated persons, particularly those who exhibit signs of impending violence, require immediate restraint.

- Verbal techniques should be tried before physical or chemical restraints are implemented.
  - Invite the person to sit down.
  - Approach the person in a nonconfrontational but attentive and receptive manner without conveying weakness or vulnerability.
  - A calm voice should be used. It is important to avoid direct eye contact or approaching the person from behind the
or moving suddenly and to stand at least one arm’s length away.

- The 3 F’s (feel, felt, found) approach responds to the persons’ emotional needs: I understand how you feel that way. Others in the same situation have felt that way, too. Most have found that talking about this feeling can help.
- If verbal techniques are unsuccessful and escalation occurs, the professional caregivers should excuse themselves and summon help.

- Physical restraints can be used when verbal techniques are unsuccessful and if there are indications for imminent harm to the person himself, to others, or to the environment. It should be performed according to an approved institutional protocol.
- Chemical restraints may be necessary, with or without physical restraints, in a person who does not respond to verbal de-escalation techniques. Rapid tranquilization may be required by benzodiazepines or neuroleptic drugs.

PLANNING FOR PREDICTABLE EMERGENCIES

Certain emergencies can be anticipated in selected patients. It is good to inform the patient and the caregivers of what might be happening and what they can do in an emergency situation (eg, calling community nurses or general practitioner, personal alarm systems, transfer from home to hospital). It is also important to discuss issues of the end of life and what is possible and what the patient wants in case of an emergency.

Advanced directives should be discussed and do-not-resuscitate orders should be available for the patient, the caregiver, and in the patient file.

In every department dealing with palliative care patients, there should be procedures and education how to handle specific palliative care emergencies. It is also necessary that the necessary medication is at hand in case of an emergency (Table 1).

REFERENCES