

European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care

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Abstract

The European Association for Palliative Care (EAPC) considers sedation to be an important and necessary therapy in the care of selected palliative care patients with otherwise refractory distress. Prudent application of this approach requires due caution and good clinical practice. Inattention to potential risks and problematic practices can lead to harmful and unethical practice which may undermine the credibility and reputation of responsible clinicians and institutions as well as the discipline of palliative medicine more generally. Procedural guidelines are helpful to educate medical providers, set standards for best practice, promote optimal care and convey the important message to staff, patients and families that palliative sedation is an accepted, ethical practice when used in appropriate situations. EAPC aims to facilitate the development of such guidelines by presenting a 10-point framework that is based on the pre-existing guidelines and literature and extensive peer review.

Introduction

Therapeutic (or palliative) sedation in the context of palliative medicine is the monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) in order to relieve the burden of otherwise intractable suffering in a manner that is ethically acceptable to the patient, family and health-care providers.

Sedation is used in palliative care in several settings:

- (1) transient sedation for noxious procedures;
- (2) sedation as part of burn care;
- (3) sedation used in end of life weaning from ventilator support;
- (4) sedation in the management of refractory symptoms at the end of life;
- (5) emergency sedation;
- (6) respite sedation;
- (7) sedation for psychological or existential suffering.

Procedural guidelines already exist for transient sedation for noxious procedures,^{1–4} in burn care⁵ and sedation

used for end of life weaning from ventilator support^{6,7} and these issues will not be addressed in this paper.

Why procedural guidelines are important

The European Association for Palliative Care (EAPC) considers sedation to be an important and necessary therapy in the care of selected palliative care patients with otherwise refractory distress. Prudent application of this approach requires due caution and good clinical practice. Inattention to potential risks and problematic practices can lead to harmful and unethical practice which may undermine the credibility and reputation of responsible clinicians and institutions as well as the discipline of palliative medicine more generally.

Potential adverse outcomes and risks of sedation in palliative care

Apart from its use for patients undergoing noxious procedures and in weaning from ventilator support, sedation is a treatment of last resort because of its anticipated adverse outcomes and potential risks.

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The anticipated adverse outcomes of sedation for the patient are impairment or loss of the ability to interact depending on the depth of sedation that is applied. This is clearly at odds with goals of care including improvement or maintenance of function (including interactional function), which, for most patients, are important and relevant goals that are valued even up to very late stages of their decline towards death.

The use of sedation to relieve patient suffering may cause distress among families⁸⁻¹² and members of the professional care team.¹²⁻¹⁵ For families, the contributing factors include: the sadness caused by the impaired ability to interact with the patient, anticipatory grief, confusion or disagreement regarding the indications for the use of sedation, and perceptions that the decision to resort to sedation was precipitous, or perhaps delayed inappropriately, or perception that sedation directly, or even indirectly, hastens death.⁸⁻¹²

Among the potential risks of sedation are paradoxical agitation,^{16,17} and hastening death. Although there are data indicating that palliative sedation does not hasten the death of patients overall,¹⁸⁻²³ a small risk of hastened death for individual patients exists (through respiratory depression, aspiration or haemodynamic compromise).²⁴ For immediately pre-terminal patients, this risk may be judged to be trivial relative to the goal of relieving otherwise intolerable suffering. In other circumstances, such as patients requesting transient respite from overwhelming symptoms, the risk of potentially hastened death may have significant, or even catastrophic, consequences. In these situations the risks of sedation may be substantial, and risk-reducing precautions (including monitoring of vital signs and the availability of antidotes) may be indicated.

Problem practices

There are many ways in which the care of patients can be undermined by the abusive, injudicious or unskilled use of sedation. Whereas there are very strong data indicating the prevalence of abuse, little is known regarding the prevalence of injudicious or substandard sedation practices.

Abuse of palliative sedation: Abuse of sedation occurs when clinicians sedate patients approaching the end of life with the primary goal of hastening the patient's death.²⁵⁻³² This has been called 'slow euthanasia'. Indeed, some physicians administer doses of medication, ostensibly to relieve symptoms, but with a covert intention to hasten death. This may occur by the deliberate use of deep sedation in patients who have no refractory symptoms, or in the deliberate use of doses that far exceed that which is necessary to provide adequate comfort. Excess doses can compromise

physiological functions such as spontaneous respiration and haemodynamic stability. These duplicitous practices represent an unacceptable, and often illegal, deviation from normative ethical clinical practice.

Injudicious use of palliative sedation: Injudicious palliative sedation occurs when sedation is applied with the intent of relieving symptoms but in clinical circumstances that are not appropriate. In this situation, sedation is applied with the intent of relieving distress and is carefully titrated to effect, but the indication is inadequate to justify such a radical intervention. The following are representative examples of injudicious use:

- (1) Instances of inadequate patient assessment in which potentially reversible causes of distress are overlooked.^{26,33}
- (2) Situations in which before resorting to sedation, there is a failure to engage with clinicians who are experts in the relief of symptoms despite their availability.^{26,34}
- (3) The case of an overwhelmed physician resorting to sedation because he is fatigued and frustrated by the care of a complex symptomatic patient.¹²
- (4) Situations in which the demand for sedation is generated by the patient's family and not the patient him/herself.¹²

Injudicious withholding of palliative sedation:

Injudicious withholding of sedation in the management of refractory distress occurs when clinicians defer the use of sedation excessively whilst persisting with other therapeutic options that do not provide adequate relief. Given the subjectivity of refractoriness and the profound interindividual variability of responsiveness to palliative interventions, these assessments are often very difficult to make. Clinicians should be aware of the potential for a 'counter phobic determination to treat' whereby anxiety about having to deal with all of the difficult discussions about sedation and end-of-life care leads to avoidant behaviours and futile therapeutic trials ultimately resulting in increased patient distress or reservations based on exaggerated concerns about hastening death.

Substandard clinical practice of palliative sedation:

This occurs in situations in which sedation is used for an appropriate indication but without the appropriate attention to one or more processes essential to good clinical care. Examples of substandard clinical practices include the following:

- (1) Inadequate consultation with the patient (if possible), family members, or other staff members to

ensure understanding of the indication for the intervention, the goals of the care plan, the anticipated outcomes, and the potential risks.

- (2) Inadequate monitoring of symptom distress or adequacy of relief.
- (3) Inadequate assessment of psychological, spiritual or social factors that may be contributing to the patient's distress.¹²
- (4) Inadequate monitoring of physiological parameters that may indicate risk of drug overdose (when clinically relevant).
- (5) Hasty dose escalation of sedative medications without titration to effect and the use of minimal effective doses.
- (6) Use of inappropriate medications to achieve sedation (i.e. opioids).^{35,36}
- (7) Inadequate care of the patient's family.¹²
- (8) Inadequate attention to the emotional and spiritual well being of distressed staff members.^{12,14}

Why a framework for procedural guidelines?

While acknowledging that specific best practices have not been rigorously developed, procedural guidelines can nonetheless be developed to provide a framework for decision making and implementation to best promote and protect the interests of patients, their families and the health-care providers administering care. The proposed framework for procedural guidelines is developed in the hope of educating medical providers, setting procedural standards for good clinical practice, promoting optimal care and conveying the important message to staff, patients and families that palliative sedation is an accepted, ethical practice when used in appropriate situations. It is also hoped that procedural guidelines may prevent or minimize the likelihood of bad outcomes that sometimes stem from substandard or unethical practices.

For all of these reasons we encourage the development and use of procedural guidelines. They may be developed or adopted at a national, local or institutional level. Irrespective, once adopted, they need to be disseminated, opened to discussion and readily available to clinicians involved in this clinical issue.

EAPC aims to facilitate the development of procedural guidelines by presenting a widely endorsed framework that is based on the pre-existing guidelines, published experience and extensive peer review.

Process of framework formulation

EAPC invited the first author to draft an initial formulation. A literature search of MEDLINE and CANCELIT were carried out for the period

1966–2008 using the terms (combination of keywords, title and text): “palliative care (KW)/ sedation (title),” terminal care (KW)/ sedation (title). These searches yielded 172 and 188 papers, respectively, including 235 distinct papers. Abstracts and full texts were reviewed and an initial formulation was drafted based on four classes of publications:

- (1) pre-existing published guidelines;^{12,19,25,37–56}
- (2) literature reviews;^{18,47,57–61}
- (3) surveys of practitioners;^{62–68} and
- (4) unpublished guidelines from individual institutions.

Expert peer review of the initial draft was invited from a wide range of palliative care clinicians both within and outside of the EAPC. Many, but not all, invitees participated actively and some did not respond. The responding peer reviewers submitted recommended points for revisions which were either linguistic, i.e. use of words or phrasing, or substantive, i.e. reflecting issues of content. Based on the recommendations of the peer reviews the draft was modified by the first author and then resubmitted for re-review.

The process of the number of cycles of re-drafting and re-reviewing was not pre-determined; rather, it ended only when there were no further substantive recommendations for changes in the substance of the framework. In all, this process of re-drafting and peer review was repeated six times. The final document was ratified and approved by the Board of the EAPC. Final modifications were made in response to the comments of the two anonymous peer reviewers of the publishing journal.

A framework for procedural guidelines

We introduce a 10-item framework that addresses the key clinical issues. The specific wording and content are proposed as recommendations. They constitute a framework, not a blueprint. The recommendations may be adopted in their current form or, preferably, modified to reflect local cultural or legal considerations or the specific needs of the context in which they will be used, be it in the home, hospital or hospice-based care.

Recommend pre-emptive discussion of the potential role of sedation in end-of-life care and contingency planning

Physicians are strongly encouraged to address end-of-life care preferences with all patients at risk of dying, particularly those with progressive terminal illness or illness characterized by intermittent life-threatening exacerbations. The scope of these discussions should be predicated on the general goals and priorities of care.

In some situations, the discussion may need to address specific issues such as CPR, ventilator support, pressor support, comfort care, antibiotics and artificial hydration and nutrition. When there are concerns about the possibility of severe distress at the end of life, these should be addressed. When it is clinically appropriate, the relief of extreme distress should be discussed. This should include discussion regarding the use of sedation as an appropriate and effective response to relieve distress when simpler measures are inadequate for the task or in emergency situations at the end of life. This is particularly relevant for patients who do not want resuscitation or ventilator support and to those for whom these interventions would be inappropriate.

When the potential for catastrophic events such as bleeding or extreme distress is foreseen, contingency plans for the management of these events should be discussed.

Outcomes of these discussions should be documented and the documentation stored in a readily accessible format. Patient and family goals and concerns should be revisited periodically, with attention paid to ongoing documentation of these discussions, even if there is no change in the plan of care.

Describe the indications in which sedation may or should be considered

Sedation is potentially indicated for patients with intolerable distress due to physical symptoms, when there is a lack of other methods for palliation within an acceptable time frame and without unacceptable adverse effects (refractoriness).

The specific intolerable symptoms should be identified. The most common symptoms include agitated delirium, dyspnoea, pain and convulsions. Emergency situations may include massive haemorrhage, asphyxiation, severe terminal dyspnoea or overwhelming pain crisis.^{69–71}

Continuous deep sedation should only be considered if the patient is in the very terminal stages of their illness with an expected prognosis of hours or days at most. Transient or respite sedation may be indicated earlier in the patient's trajectory to provide temporary relief whilst waiting for treatment benefit from other therapeutic approaches.

Occasionally, when patients approach the end of life, sedation may be considered for severe non-physical symptoms such as refractory depression, anxiety, demoralization or existential distress.^{72–78} There is no consensus on the appropriateness of sedation for these indications.⁵⁴ Special precautions for these clinical circumstances are presented in Appendix 1.

Describe the necessary evaluation and consultation procedures

Extreme distress is a medical emergency and patient evaluation must be performed with due urgency.

The patient must be evaluated by a clinician with sufficient experience and expertise in palliative care. If the evaluation is carried out by a trainee, it should be corroborated by a senior physician with expertise in palliative medicine, a palliative medicine expert or a palliative care team. Wherever possible this evaluation should be interdisciplinary.

The evaluation should include:

- (1) the patient's medical history;
- (2) all relevant investigations; and
- (3) a physical examination of the patient.

In particular, evaluation should exclude acute deterioration caused by a treatable complication of illness such as sepsis, a reversible metabolic event, medication toxicity and common events such as pleural effusion, pericardial tamponade, ureteric obstruction, upper airway obstruction, gastrointestinal obstruction, active bleeding, urinary retention or elevated intracranial pressure.

The assessment should evaluate any psycho-social and environmental factors, including sources of spiritual or existential distress, which may be adversely affecting the level of distress. Input should be sought from the involved psycho-social health-care providers, nursing staff, family and any other relevant sources. All efforts should be made to involve the patient's primary physician in the assessment process and in any recommendations.

The assessment should include estimates as to whether death is anticipated within minutes to hours, hours to days, days to weeks, or longer. This prognostic assessment should be based on the extent of disease, validated prognostic instruments, rate of decline in functional status, presence or absence of vital organ failure, and the presence or absence of adverse prognostic factors such as very poor performance status, dyspnoea, anorexia, degree of oral intake, delirium and oedema.

The assessment must evaluate the patient's capacity to make decisions about ongoing care. This should be based on standard criteria such as:

- (1) the patient can express their own will;
- (2) the patient can understand the relevant information;
- (3) the patient can understand and acknowledge the implications of their choice.

If decisional capacity is in doubt, then the expert evaluation by a psychiatrist may be required.

If there is uncertainty in the patient evaluation, especially with regards to whether all options to relieve distress have been considered, consultation with experts (e.g. psychiatrists, anaesthetists, pain specialists, oncologists and specialist nurses) should be sought.

Whenever possible, the medical rationale for sedation as well as the decision-making process should be based on input from the multi-professional palliative care team, rather than by the treating physician alone. Case discussion and team conferences may be suitable platforms to facilitate this process.

The medical rationale for recommending sedation, the decision-making process, the aims of sedation and the planned depth and duration of sedation should be recorded, in any easily retrieved document (e.g. the patient's medical record).

Specify consent requirements

In non-critical situations in the management of patients with decisional capacity, the aims, benefits and risks of the proposed sedation should be discussed including reference to the following:

- (1) The patient's general condition including the cause of the intolerable distress, treatments that have been attempted, limitations of other options of care and, when relevant, limited anticipated survival.
- (2) The rationale for the decision that sedation is the only method available for achieving symptom relief within an acceptable time frame.
- (3) The aims of sedation.
- (4) The method of sedation, including the depth of planned sedation, patient monitoring, possibility of planned weaning (in some circumstances), with an option to discontinue sedation (in some circumstances).
- (5) The anticipated effects of sedation including degree of reduction in consciousness levels, estimated effects on mental activities, communication and oral intake.
- (6) The potential uncommon risks such as paradoxical agitation, delayed or inadequate relief, and the possibility of complications including hastened death.
- (7) Medical treatments and nursing care to be maintained during sedation: treatments and care to maximize patient comfort are continued and the patient's and their family's wishes are respected.
- (8) The expected outcomes if sedation is not performed including other treatment options, degree of suffering likely to persist with each option and expected survival with each option.
- (9) Commitment to the patient's well being and provision of best possible care irrespective of patient treatment choices.

With the permission of the patient, it is generally preferable to conduct this discussion with the participation of significant family members. This approach maximizes communication and often facilitates important meaning-related discussions between patients and their families while the opportunity still exists.

The content and conclusions from the discussion should be documented in the patient's medical record.

If the patient lacks decisional capacity and there is no advanced directive, permission needs to be obtained from a legally recognized proxy. The treating clinicians should emphasize that the role of the proxy or family is not to decide, but rather it is to indicate what the patient would have wanted and the reasoning that leads them to their conclusion. It should be emphasized to the family that they are not being asked to make a decision, and that the professional care team takes the responsibility for the medical decision. (This section needs to be consistent with local regulations.)

In the care of terminally ill patients who have no advanced directive and no health-care proxy and who are in severe distress whilst actively dying, provision of comfort measures (including, if necessary, the use of sedation) is the 'standard of care' and should be the default strategy for clinician treatment decisions.

Indicate the need to discuss the decision-making process with the patient's family

In situations in which the family members were not part of the consent process, permission should be sought to communicate the decision with the patient's family. Informing the family should be presented to the patient as usual practice and permission sought in the form of assent.

With the patient's assent, discussion should be held with the family to inform them of the patient's condition, treatment options, potential outcomes of those treatment options and the consequences of a patient's expressed preferences. It is often helpful to conduct part of the discussion with the patient's participation and part to address the family's concerns alone.

In the uncommon event of patients not permitting discussion with their family, the reasons should be explored and the patients should be strongly encouraged to reconsider their decision. In some cases this may include the need to counsel them about the

potential distress that withholding of information may cause to family members.

In some cultures family assent may be deemed necessary or desirable. When this is the case and family members do not assent to the treatment plan, the care team should:

- (1) provide sufficient information to help families better understand the patient's conditions and suffering;
- (2) support the patient and their family by talking with each party and finding a solution that is acceptable to both; and
- (3) provide psychological support to families to relieve them of factors that contribute to conflicts, such as grief and guilt.

While the patient and their family continue to discuss the decision, the care team should explore treatment options that maximally respect the patient's will and benefits.

Present direction for selection of the sedation method

In general, the level of sedation should be the lowest necessary to provide adequate relief of suffering. Other than in emergency situations at the end of life, intermittent or mild sedation should generally be attempted first. For some patients, a state of 'conscious sedation', in which the ability to respond to verbal stimuli is retained, may provide adequate relief without total loss of interactive function.

Doses can be titrated down to re-establish lucidity after an agreed interval to re-evaluate the patient's condition and preferences regarding sedation or for pre-planned family interactions (this, of course, is a potentially unstable situation, and the possibility that lucidity may not be restored promptly, that the refractory symptoms may reappear or that death may ensue should be explained to both the patient and family).

Deeper sedation should be adopted when mild sedation has been ineffective.

Continuous deep sedation could be selected first if:

- (1) the suffering is intense;
- (2) the suffering is definitely refractory;
- (3) death is anticipated within hours or a few days;
- (4) the patient's wish is explicit; and
- (5) in the setting of an end-of-life catastrophic event such as massive haemorrhage or asphyxia.

Present direction for dose titration, patient monitoring and care

Medications suitable for sedation in palliative care are presented in Appendix 2.

Whenever possible, sedation should be started by a physician and a nurse together. Preferably, it should be carried out or supervised by clinicians with leadership roles and experience in end-of-life care (senior physicians and or nurses) so as to reinforce the weightiness of the intervention and the message that excellence in palliation is a priority. Initially, the patient should be assessed at least once every 20 minutes until adequate sedation is achieved, and subsequently at least three times per day after adequate sedation has been achieved.

The severity of suffering, level of consciousness and adverse effects related to sedation (such as delirium, agitation or aspiration) should be evaluated regularly. The doses of the medications should be increased or reduced gradually to a level at which suffering is palliated with a minimum suppression of the consciousness levels and undesirable effects, with documentation of the reason for changes and response to such manoeuvres. Consciousness is assessed by the patient's response to stimuli, agitation or motor activity, and facial expression. Examples of scales to help assess pain and distress in patients with lowered consciousness are presented in Appendix 3.

When sedation is intended to be short term, intermittent or light, efforts should be made to preserve physiological stability within the pre-agreed treatment constraints. The level of sedation and routine physiological parameters such as heart rate, blood pressure and oxygen saturation should be monitored regularly. If the patient experiences heavy snoring and abrupt onset of apnoea, the dose of sedative should be decreased. If obtundation with respiratory depression occurs in a patient undergoing respite sedation, and the situation is life threatening, careful administration of a benzodiazepine antagonist (flumazenil) may occasionally be indicated and appropriate to re-establish patient stability.

When the goal of care is to ensure comfort until death for an imminently dying patient, the only critical parameters for ongoing observation are those pertaining to comfort. Observations of heart rate, blood pressure and temperature do not contribute to the goals of care and should be discontinued. Respiratory rate is monitored primarily to ensure the absence of respiratory distress and tachypnoea. Since downward titration of drug doses places the patient at risk for recurrent distress, in most instances it is not recommended even as the patient approaches death. In dying patients, gradual deterioration of respiration is expected and alone should not constitute a reason to decrease sedation.

In all cases, the care team must maintain the same level of humane dignified treatment as before sedation; this level of care includes talking to patients and adjustment of the environment. Oral care, eye care, toilet, hygiene and pressure wound care should be performed on the basis of the patient's wishes and the estimated risks/harms in terms of the goals of care.

Guidance for decisions regarding hydration and nutrition and concomitant medications

The decision about artificial hydration/nutrition therapy is independent of the decision about sedation itself. Whether artificial hydration/nutrition therapy is performed should be individually decided through comprehensive evaluation of the patient's wishes and the estimated benefits/harms in light of the treatment aim (palliation of suffering).

Opinions and practices vary. This variability reflects the heterogeneity of attitudes of involved clinicians, ethicists, patients, families and local norms of good clinical and ethical practice.

Individual patients, family members and clinicians may regard the continuation of hydration as a non-burdensome humane supportive intervention that represents (and may actually constitute) one means of reducing suffering. Alternatively, hydration may be viewed as a superfluous impediment to inevitable death that can be appropriately withdrawn because it does not contribute to patient comfort or the prevailing goals of care.

Often, the patient will request relief of suffering and give no direction regarding hydration and nutrition. Under these circumstances, family members and health-care providers must work to reach a consensus on what constitutes a morally acceptable plan based on the patient's best interests

If adverse effects of artificial hydration and or nutrition therapy exacerbate patient suffering, then reduction or withdrawal of artificial hydration/nutrition should be considered.

Medications for symptom palliation used before sedation should be continued, unless they are ineffective or have distressing side effects. Medications that are either inconsistent with or, irrelevant to, the goal of patient comfort may be withdrawn generally. In most cases opioids should be continued, possibly with dose modification, unless adverse effects or signs of overdose (e.g. respiratory depression or myoclonus) are observed. If symptoms are well palliated and overdose signs are observed, opioids doses should be reduced, but should not be withdrawn rapidly, owing to the risk of precipitating withdrawal.

The care and informational needs of the patient's family

Situations in which a family member is sedated are often profoundly distressing to family members. Families should be allowed and encouraged to be with the patient and, in many situations, an opportunity to say goodbye may be of critical importance. If the patient is

hospitalised, every effort should be made to provide privacy for emotional and physical intimacy. Visitation restrictions should be minimized, especially for children. To promote the family's sense of well being and peacefulness, consideration should be given to the aesthetics of the care environment, including the availability of basic supports for the family such as tissues, chairs, water, access to a telephone, and opportunity to sleep in the room or nearby.

The care team must provide supportive care to the members of the patient's family. This includes listening to families' concerns, attention to grief and physical/psychological burdens and guilt. The care team should counsel the family in the ways that they can continue to be of help to the patient, for instance by being with, talking to and touching the patient, providing mouth care, and managing the atmosphere of the patient's care (e.g. providing the patient's favourite music, scents, singing favourite songs, saying prayers or reading to the patient).

Families of sedated patients need to be kept informed about the patient's well being and what to expect. The care team should provide regular information updates to the family including the patient's condition, degree of suffering, anticipated changes or, when appropriate, notification that death is approaching and what can be expected in the dying process.

Families often need repeated reassurance that other methods have been sufficiently trialled and/or carefully considered but were ineffective, that sedation is unlikely to shorten the patient's life, and that sedation can be discontinued or reduced if needed.

After the death of the patient, the family should be offered the opportunity to meet with the care providers to give them the opportunity to ventilate grief and to discuss any outstanding concerns that they may harbour about the care delivered in the last days of life.

Care for the medical professionals

Situations in which a patient is sedated can often be profoundly distressing to staff members. This is particularly true if there is discord regarding the appropriateness of the intervention and in situations when the process is protracted.

The care team should recognize the potential for staff distress. All participating staff members need to understand the rationale for sedation and goals of care. Whenever possible this should be addressed at team meetings or case conferences, both before and after the event, to discuss the professional and emotional issues related to such decisions and to improve local procedures when necessary.

Distress can be mitigated by fostering a culture of sensitivity to the emotional burdens involved in care, participating in the deliberative processes leading up to a treatment decision, sharing information and engaging in multidisciplinary discussions that offer the group or individuals opportunities to vent their feelings.

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Appendix I: Special considerations for the use of sedation in situations of refractory existential or psychological distress

Rationale for special considerations

Sedation in the management of refractory psychological symptoms and existential distress is different from other situations for four major reasons:

- (1) by virtue of the nature of the symptoms being addressed, it is much more difficult to establish that they are truly refractory;
- (2) the severity of distress of some of these symptoms may be very dynamic and idiosyncratic, and psychological adaptation and coping is common;
- (3) the standard treatment approaches have low intrinsic morbidity; and
- (4) the presence of these symptoms does not necessarily indicate a far advanced state of physiological deterioration.^{73,77,78}

Special guidelines

- (1) This approach should be reserved for patients in advanced stages of a terminal illness.
- (2) The designation of such symptoms as refractory should only be done following a period of repeated assessment by clinicians skilled in psychological care who have established a relationship with the patient and their family along with trials of routine approaches for anxiety, depression and existential distress.
- (3) The evaluation should be made in the context of a multidisciplinary case conference, including representatives from psychiatry, chaplaincy and ethics, as well as those providing care at the bedside, because of the complexity and frequently multifactorial nature of this situation.
- (4) In the rare situations that this strategy is indeed appropriate and proportionate to the situation, it should be initiated on a respite basis for 6–24 hours with planned downward titration after a pre-agreed interval.
- (5) Continuous sedation should only be considered after repeated trials of respite sedation with intensive intermittent therapy have been performed.

Appendix 2: Examples of drugs used for sedation in palliative care

Benzodiazepines

Benzodiazepines reduce anxiety and cause amnesia, they have a synergistic sedative effect with opioids and anti-psychotics, they are anticonvulsants and may help prevent the development of pre-morbid seizures. They can all cause paradoxical agitation, respiratory depression, and withdrawal if the dose is rapidly reduced after continual infusion and tolerance. Flumazenil is a short half-life benzazepine antagonist.

Midazolam

General: Midazolam is the most commonly used agent.

Pharmacology: Water soluble, short-acting benzodiazepine. Metabolised to a lipophilic compound that rapidly penetrates the central nervous system. Brief duration of action because of rapid redistribution, therefore administration by continuous infusion is generally required to maintain a sustained effect.

Advantages: Rapid onset. Can be administered intravenously (IV) or subcutaneously (SC).

Starting dose: 0.5–1 mg/hr, 1–5 mg as needed.

Usual effective dose: 1–20 mg/hr.

Lorazepam

General: Intermediate-acting benzodiazepine that has a peak effect approximately 30 min after intravenous administration. It is less amenable to rapid titration up or down than midazolam, because of its slower pharmacokinetics.

Pharmacology: Elimination is not altered by renal or hepatic dysfunction.

Advantages: Rapid onset. Can be administered IV or SC.

Starting dose: 0.05 mg/kg every 2–4 hr when administered by intermittent bolus.

Flunitrazepam

General: Water-soluble long half-life benzodiazepine.

Pharmacology: Elimination is not altered by renal or hepatic dysfunction.

Advantages: Rapid onset. Can be administered IV or SC.

Disadvantage: Slow washout due to long half-life.

Starting dose: A bolus dose of 1–2 mg, continuous infusion 0.2–0.5 mg/hr.

Neuroleptics/antipsychotics

Neuroleptics may be effective sedatives particularly if the patient is manifesting signs and symptoms of delirium. Delirium is an acute confusional state that can be difficult to differentiate from anxiety, yet the distinction is important, because the administration of opioids or benzodiazepines as initial treatment for delirium can worsen the symptom.

Levomepromazine (methotrimeprazine)

General: Levomepromazine is an antipsychotic phenothiazine.

Advantages: Rapid onset, antipsychotic effect in cases of delirium, some analgesic effect, can be administered orally or parenterally (IV, SC or intramuscularly (IM)).

Starting dose: stat dose 12.5–25 mg and 50–75 mg continual infusion.

Usual effective dose: 12.5 or 25 mg q8h and q1h prn for breakthrough agitation or up to 300 mg/day continual infusion.

Adverse effects: Orthostatic hypotension, paradoxical agitation, extrapyramidal symptoms, anticholinergic effects.

Chlorpromazine

General: Widely available antipsychotic can be administered orally, parenterally (IV or IM) and rectally.

Advantages: Antipsychotic effect for delirious patients.

Starting dose: IV or IM 12.5 mg q 4–12 hours, or 3–5 mg/hour IV or 25–100 mg q 4–12 hours PR.

Usual effective dose: Parenteral 37.5–150 mg/day, PR 75–300 mg/day.

Adverse effects: orthostatic hypotension, paradoxical agitation, extrapyramidal symptoms, anticholinergic effects.

Barbiturates

Barbiturates reliably and rapidly cause unconsciousness and, since their mechanism of action differs from the opioids and benzodiazepines, they may be useful in patients who have developed extreme levels of tolerance to these other medications. They do not have an analgesic effect, so opioids will probably be necessary for patients with pain.

Pentobarbital

General: Barbiturate.

Advantages: Rapid onset, anticonvulsant.

Dose: Loading dose: 2–3 mg/kg slow intravenous push (no faster than 50 mg/min); at time of loading dose, start infusion at 1–2 mg/kg/hr; titrate to desired level of sedation.

General anaesthetics

Propofol^{79,80}

General: Short acting general anaesthetic.

Advantages: Quick onset of sedation, ability to rapidly titrate, rapid washout.

Adverse effects: Hypotension and respiratory depression, pain on infusion into small peripheral veins.

Precautions: Use strict aseptic technique when administering propofol. Change infusion tubing every 12 hours. Discard vial and any unused drug if not fully infused after 12 hours.

Non-sedative benefits: antiemetic, antipruritic and bronchodilatation.

Starting dose: 0.5 mg/kg/hr.

Usual dose: 1–4 mg/kg/hr.

Appendix 3: Scales to help assess distress in patients with lowered consciousness

Critical-Care Pain Observation Tool (CCPOT)

Indicator	Description	Score	
Facial expression	No muscular tension observed	Relaxed, neutral	0
	Presence of frowning, brow lowering, orbit tightening and levator contraction	Tense	1
	All of the above facial movements plus eyelid tightly closed	Grimacing	2
Body movements	Does not move at all (does not mean the absence of pain)	Absence of movements	0
	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection	1
	Pulling tube, attempting to sit up, moving limbs, thrashing about, not following commands, striking at staff, trying to climb out of bed	Restlessness	2
Muscle tension (evaluate by passive flexion and extension of upper extremities)	No resistance to passive movements	Relaxed	0
	Resistance to passive movements	Tense, rigid	1
	Strong resistance to passive movements, inability to complete them	Very tense or rigid	2
Compliance with the ventilator (for intubated patients)	Alarms not activated, easy ventilation	Tolerating ventilator or movement	0
	Alarms stop spontaneously	Coughing but tolerating	1
Or			
Vocalization (for non-ventilated patients)	Asynchrony: blocking ventilation, alarms frequently activated	Fighting ventilator	2
	Talking in normal tone or no sound	Talking in normal tone or no sound	0
	Sighing, moaning	Sighing, moaning	1
	Crying out, sobbing	Crying out, sobbing	2
Total possible score (range)			0–8

Note that the higher the total score, the greater the pain level.

Adapted from: Gelinas C, Fillion L, Puntillo KA, Viens C, Fortier M. Validation of the critical-care pain observation tool in adult patients. *Am J Crit Care* 2006; 15: 420–427 with permission from the American Association of Critical-Care Nurses.⁸¹

Richmond agitation sedation scale (RASS)*

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to <i>voice</i> (≥10 seconds)	} Verbal stimulation
-2	Light sedation	Briefly awakens with eye contact to <i>voice</i> (<10 seconds)	
-3	Moderate sedation	Movement or eye opening to <i>voice</i> (but no eye contact)	} Physical stimulation
-4	Deep sedation	No response to <i>voice</i> , but movement or eye opening to <i>physical</i> stimulation	
-5	Unarousable	No response to <i>voice or physical</i> stimulation	

Procedure for RASS assessment

1. Observe patient
 - a. Patient is alert, restless, or agitated. (score 0 to +4)
2. If not alert, state patient's name and say to open eyes and look at speaker.
 - b. Patient awakens with sustained eye opening and eye contact. (score -1)
 - c. Patient awakens with eye opening and eye contact, but not sustained. (score -2)
 - d. Patient has any movement in response to voice but no eye contact. (score -3)
3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.
 - e. Patient has any movement to physical stimulation. (score -4)
 - f. Patient has no response to any stimulation. (score -5)

Reproduced from Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation–Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002; 166: 1338–1344 with permission from the American Thoracic Society.⁸²

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