Palliative sedation (PS) is the use of medications to induce decreased or absent awareness in order to relieve otherwise intractable suffering at the end of life. Although uncommon, some patients undergoing aggressive symptom control measures still have severe suffering from underlying disease or therapy-related adverse effects. In these circumstances, use of PS is considered. Although the goal is to provide relief in an ethically acceptable way to the patient, family, and health care team, health care professionals often voice concerns whether such treatment is necessary or whether such treatment equates to physician-assisted suicide or euthanasia. In this review, we frame clinical scenarios in which PS may be considered, summarize the ethical underpinnings of the practice, and further differentiate PS from other forms of end-of-life care, including withholding and/or withdrawing life-sustaining therapy and physician-assisted suicide and euthanasia.

**Selection of Appropriate Patient Candidates**

Palliative sedation is used at the end of life to relieve an unacceptable degree of suffering that is refractory to other therapies or when other therapies are estimated to be unhelpful in the given time frame. Palliative sedation is used when traditional opioid-based therapies are either inadequate to control suffering or cause unacceptable adverse effects. Often, PS is used to treat delirium, pain, dyspnea, nausea, or other physical symptoms. Palliative sedation may be considered when patients or surrogate decision makers have given informed consent and generally when consensus exists among patients, families, and staff about the appropriateness of the therapy.

**Selection of Pharmacological Agents**

When choosing pharmacological agents for PS, the physician faces a number of considerations. Some medications have recently received negative attention in the press, including use of propofol in the death of popular singer Michael Jackson, and use of barbiturates in physician-assisted suicide and capital punishment. When studying the aftermath of Hurricane Katrina, reviewers concluded that physicians’ choice of benzodiazepines instead of barbiturates indicated a goal of palliation rather than euthanasia, citing that barbiturates were more “deadly.” Negative press may contribute to restrictive institutional policy and difficulty in accessing these medications for therapeutic use.

Most centers use a midazolam-based regimen for PS because of the drug’s short half-life, relatively benign adverse effects, ease of intravenous or subcutaneous administration.

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Dr Mueller is a member of the Boston Scientific Patient Safety Advisory Board and is an Associate Editor of Journal Watch General Medicine, but neither of these activities is related to the article.

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tion, and generally good efficacy. Other programs that use primarily barbiturates, either alone or in combination with other agents, have also reported good results. Our institution (Mayo Clinic, Rochester, MN) supports the use of ketamine or propofol in patients whose condition is refractory to opioids and midazolam. Opiates should not be used for the primary purpose of sedation, but rather should be continued adjunctively during PS for analgesic purposes and to prevent opiate withdrawal.

**Choice of Overseeing Practitioners**

When available, palliative medicine teams should be involved when PS is practiced, given their familiarity with advanced PS therapies, if necessary. Palliative medicine physicians can consider consulting with other experienced colleagues, ethics consultants, and legal departments as needed for consensus when clinical circumstances are unique (ie, when the patient, patient’s family members, or staff disagree about the use of PS). Other disciplines, including chaplaincy, psychiatry, social work, and other organ- or disease-specific specialists, may be involved on as-needed basis. For refractory suffering or concern regarding adverse effects, consulting anesthesiology teams can be considered. However, routine involvement is generally unnecessary.

**Level of Sedation**

Clinicians should use the minimal dose of sedatives needed to achieve acceptable relief of suffering. This technique helps minimize the risk of untoward adverse effects and maximize the chance of maintaining interactive capability with family and health care professionals during PS. The sedation level should be balanced according to the patient or surrogate’s value placed on the effectiveness of symptom relief, perceived benefits of such relief, and the burden of adverse effects, including reduced or absent ability to interact.

**Continuous vs Intermittent Sedation**

In most of the literature, PS refers to continuous sedation until death. However, in some instances, intermittent PS has been used to serve as a respite for a patient, with planned discontinuation of PS at an agreed-on time. Investigators have reported improvement in symptoms with achievement of interactive function afterward, but this practice is less-well described than continuous sedation until death.

**Non-Physical Suffering**

Usually, PS is used to treat physical symptoms, including delirium, dyspnea, and pain, most commonly. Several studies have reported use of PS for fatigue and malaise; however, whether these symptoms represent existential or physical suffering is debatable. A few studies have directly addressed the use of PS for existential or psychological suffering. Indeed, non-physical suffering is legitimate and needs to be recognized, but this can pose a challenging therapeutic quandary given the difficulty in differentiating between appropriate responses to illness and psychopathologies such as depression. Patients requesting PS for existential suffering represent a small subset of cases, and the issue remains controversial.

**Ideal Practice Setting**

In many institutions, sedation is confined to intensive care units and operating rooms for purposeful transient unawareness during noxious procedures, and is accompanied by cardiac monitoring. Thus, sedation without cardiac monitoring on general hospital services represents a paradigm shift and may be met with resistance. Because intensive care units are specially equipped and attended by highly specialized staff with the goal of preserving life, these rooms are in high demand and should be reserved for the critically ill whose primary goal is survival. Furthermore, the intensive care setting can be hectic and uncomfortable for families. For those who prioritize comfort at the time of inevitable death, intensive care units are generally a suboptimal setting for PS. If, however, goals of care shift from life prolongation to comfort and a short interval to death precludes transfer from the intensive setting, PS can be effectively implemented in this setting. Palliative sedation should be conducted in general care areas or inpatient palliative care or hospice settings, with monitoring of observed levels of comfort and signs of untoward adverse effects. Cardiac monitoring is not helpful for achieving the goals of patients receiving PS and should be avoided, because it adds stress and expense for families and distracts loved ones from attending to the dying patient.

Although a variety of parenteral (intravenous or subcutaneous), oral, or rectal medications can be used for PS, not all patients requiring PS are in the inpatient hospital or hospice setting. Palliative sedation can be used in the home setting, and studies have demonstrated promising results using intravenous midazolam infusion protocols safely and effectively in that setting. Although beyond the scope of this review, further research regarding in-home PS is needed.

**Ethical Issues**

Palliative sedation represents a part of the spectrum of good clinical practice when used in the appropriate circumstances. The US Supreme Court has supported the right of informed patients to pursue relief of suffering, even if the treatment may unintentionally shorten life. Although PS is legally sound, ethical tension often centers around the fol-
lowing topics: the distinction of PS from physician-assisted suicide and euthanasia, the unavoidable morbidity (loss of social function and risk of life-shortening adverse effects) of PS, and the relationship between refusing artificial nutrition and hydration (ANH) and PS.

**Distinction of PS from Physician-Assisted Suicide and Euthanasia**

Distinguishing PS from physician-assisted suicide and euthanasia calls on the ethical principles of beneficence (duty to alleviate suffering) and non-maleficence (duty to prevent or avoid harm). Palliative sedation differs from physician-assisted suicide and euthanasia by intent and outcome (Table). Although physician-assisted suicide is legal in some states, euthanasia is illegal throughout the United States. The intent of PS is relief of unremitting and intractable suffering achieved by sedation, whereas the intent of physician-assisted suicide and euthanasia is termination of the patient’s life. The desired outcome of physician-assisted suicide and euthanasia is patient death. In contrast, the desired outcome of PS is relief of suffering through sedation, with the possible risk of hastening death. This practice has been traditionally justified by the doctrine of double effect (see subsequent discussion). However, studies have affirmed that a very small minority of patients sedated at end of life experience life-threatening adverse effects such as aspiration or respiratory depression. Furthermore, recent prospective and retrospective data suggest that in the overwhelming majority of patients, PS at end of life does not hasten death. Thus, it can be argued that PS does not cause or hasten death. Although the outcome of PS may include death as a product of disease, death is not a criterion for successful PS, whereas in physician-assisted suicide and euthanasia, death is the desired criterion for success.

**Morbidity of PS and the Doctrine of Double Effect**

As previously mentioned, evidence suggests that in most cases PS does not shorten life; rather, the underlying illness itself results in death. When facing the clinical decision to use PS or not, physicians are still confronted with the theoretical risk of life-shortening untoward adverse effects of sedation, as well as the foreseen likelihood of loss of social interaction of the patient. Thus, physicians may experience ethical tensions among beneficence, non-maleficence, and respect for the patient’s autonomy. When facing these decisions, palliative medicine physicians often cite the doctrine of double effect in PS practice. The doctrine of double effect is grounded in the ethical principle of proportionality. It originated from Thomas Aquinas in the 13th century. This doctrine asserts that, an action in the pursuit of a good outcome is acceptable, even if it achieved through means with an unintended but foreseeable negative outcome, if that negative outcome is outweighed by the good outcome. When applied to the use of PS, relief of intolerable symptoms (desired good outcome) through use of medications that will likely cause loss of social interaction and may hasten death (unintentional but foreseeable possible consequence) is ethically acceptable, given that certain conditions are met. Those conditions include that the action (sedation) is morally good or neutral, the undesired outcome (loss of interactional function and potentially hastened death) is not directly intended, the desired effect is not necessarily a direct result of the unintended negative result (in other words that symptom relief can be achieved without the death of the patient), and that the good effect is proportional to the negative effect.

**Refusal of ANH During PS**

Another important ethical tension surfaces with the decision of whether to continue ANH during PS. Some may conclude that PS requires administration of ANH because the patient cannot eat or drink. Others have raised the concern that discontinuing ANH during PS may become the cause of the patient’s death. The ethical issues of PS and simultaneous refusal of ANH are complex, and opinions and treatment practices vary. Some argue that continuing ANH prevents suffering on some level, and others argue that it is an unnecessary burden with no clear symptom benefit. No clear evidence shows that providing ANH prolongs life in imminently dying patients. Likewise, a number of studies report no survival benefit with ANH in terminally ill but not yet moribund populations. Although it is not evident that ANH prolongs life in dying patients, ANH is considered by many clinicians as a form of life-prolonging treatment, likely due to the life-sustaining benefit of ANH in other clinical settings. Additionally, court rulings have upheld ANH as potentially life-sustaining treatments.

Of note, many patients receiving PS have already stopped all forms of nutrition and hydration for physiological reasons before PS is begun. When a dying patient is still receiving ANH and develops refractory symptoms necessitating PS, ANH may be continued or discontinued according to the patient’s goals and cultural beliefs. Use of ANH should be addressed with patients or surrogates as part of the larger informed consent discussions, and, as in all instances of practicing PS, physician intent to relieve suffering, not to shorten life, should be clearly documented. Guidelines for addressing these issues have been published. When consensus in the care team or family is lacking, review by a multidisciplinary team including ethics consultation may be appropriate, when available. Even if continuing ANH clearly prolonged life in the imminently dying, refusal of ANH would still have inde-
TABLE. End-of-Life Decision Making and Respective Cause of Death, Intention of Intervention, and Legality of Treatments

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Intent/goal of intervention</th>
<th>Legal?</th>
<th>Withdraw life-sustaining treatment</th>
<th>Withhold life-sustaining treatment</th>
<th>Palliative sedation and analgesia</th>
<th>Physician-assisted suicide</th>
<th>Euthanasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid burdensome intervention</td>
<td>Underlying disease</td>
<td>Yes⁵</td>
<td>Underlying disease</td>
<td>Yes⁶</td>
<td>Underlying disease⁴</td>
<td>Intervention prescribed by physician and used by patient</td>
<td>Intervention used by physician</td>
</tr>
<tr>
<td>Remove burdensome intervention</td>
<td>Underlying disease</td>
<td>Yes⁶</td>
<td>Underlying disease</td>
<td>Yes⁶</td>
<td>Underlying disease⁴</td>
<td>Intervention prescribed by physician and used by patient</td>
<td>Intervention used by physician</td>
</tr>
</tbody>
</table>

⁴ Note doctrine of double effect.
⁵ A number of states limit the power of surrogate decision makers regarding life-sustaining treatment.
⁶ Legal only in Oregon, Washington, and Montana.

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pendent ethical validation under the larger issue of refusing life-sustaining treatments. The right of patients to refuse or request withdrawal of life-sustaining treatment has been upheld in US courts, including the Supreme Court.2,3,5,6 (Table).20 These cases have established that no treatment has unique moral status and that ANH are medical treatments, not basic care. Thus, withdrawal or withholding ANH is ethically equivalent to refusing any other treatment as long as the patient or surrogate makes an informed choice and intent is removal of a burdensome intervention.

Ethical soundness of refusing life-sustaining therapy is based on the principles of non-maleficence and respect for patient autonomy. Although the outcome of refusing any life-sustaining treatment may be death from disease, the intent is to remove a treatment that may be causing harm or is perceived by the patient as burdensome and to honor the patient’s right to be left alone if desired.3 These decisions are often complex but can be framed in terms of the benefit of treatment from the patient’s point of view, effectiveness of the intervention based on objective data, and burdens of the treatment.3,5 If patients or surrogates assert that the perceived burden of a treatment outweighs the potential benefit or effectiveness of treatment, the treatment should be discontinued.

SUMMARY

Palliative sedation has an important place on the continuum of appropriate palliative care at the end of life. It is appropriate therapy for refractory and unacceptably severe suffering. As with any other therapy, the patient or surrogate should be informed of potential adverse effects, including loss of social interaction and potential for life-threatening aspiration or respiratory depression. Palliative medicine teams should be involved, if possible, in any case in which PS is considered. Institutional lack of palliative medicine availability should not preclude the use of PS when appropriate. Procedural guidelines have been published elsewhere.

At the end of life, patient goals often shift to comfort, and removal of burdens and relief of suffering become paramount. Many physicians are uncomfortable removing life-sustaining therapy or providing comfort-directed medication because of confusion about the ethical soundness of such treatments. In contrast to physician-assisted suicide or euthanasia, withdrawal of or withholding life-sustaining treatment and PS are ethically sound options. We hope that by increasing familiarity with the ethical basis for these practices, this review will encourage their appropriate application.

We acknowledge W. David Mauck, MD, of the Department of Anesthesiology, Division of Pain Medicine, for his contribution to concepts in this article.

REFERENCES


CME Questions About Palliative Sedation

1. A 61-year-old woman with metastatic breast cancer is hospitalized for dyspnea. She has symptomatic pleural effusions with lung, brain, and bone metastases. The pleural effusions are drained, and morphine initiated at 6 mg per hour resolves her dyspnea and hypoxia. That night the patient clearly shows signs of imminent death and develops agitated terminal delirium, which does not respond to haloperidol and other supportive cares. Her family knows she will die soon and wants her to be comfortable, no matter what. Which one of the following is the next most appropriate step?

a. Continue morphine infusion and titrate up until the patient is sedated and appears comfortable
b. Start midazolam infusion and discontinue morphine because the patient will no longer need it
c. Continue scheduled morphine at current dose and start midazolam infusion until the patient no longer appears agitated or distressed
d. Refuse to use sedation because agitated delirium is not an ethically sound indication
e. Ask for ethics consultation

2. A 73-year-old man with a history of ventricular dysrhythmia and an implanted cardioverter defibrillator (ICD) is admitted to the intensive care unit. He has developed sepsis with resultant renal failure and has had a stroke in the setting of disseminated intravascular coagulation. The patient’s wife (next of kin) requests that you deactivate the ICD because she is concerned that her husband will experience shocks during the dying process. Other family members agree, but there is no advance directive. Which one of the following is the next most appropriate clinical step?

a. Refuse to comply with ICD deactivation since there is no advance directive
b. Obtain an ethics consultation to discuss permissibility of ICD deactivation
c. Call the hospital legal department for advice
d. Deactivate the ICD in compliance with the family’s stated wishes
e. Refuse to comply because granting the request is akin to euthanasia

3. A 79-year-old man with widely metastatic colon cancer is admitted to the hospital for intractable nausea and pain, and is found to have a complete bowel obstruction. He is not an operative candidate, and his condition is considered “terminal.” The patient’s pain is well controlled with opiates, and he is conversant. His surgeon recommends total parenteral nutrition and intravenous fluids, but the patient does not want these started because he suggests such measures would be “prolonging the dying process.”

Which one of the following is the best answer?

a. Obtain a psychiatry consultation to determine if the patient has decision-making capacity or if his judgment is impaired because of suffering and distress
b. Ask the court to review the case to see if emergency guardianship can be obtained because you have determined that the patient does not have decision-making capacity if he is refusing life-sustaining therapy

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c. Ask other family members to convince the patient that his request is morally wrong and attempt to convince him otherwise

d. Consult the legal department because granting this request is akin to physician-assisted suicide or euthanasia

e. Ensure that the patient is informed and that he understands the result of not starting ANH, and, if so, comply with his wish

4. A 29-year-old woman is admitted with melanoma widely metastatic to the brain and pericardium, and she has several skeletal lesions. A 10-cm tumor is compressing the patient’s brachial plexus, causing excruciating pain in her neck, arm, and shoulder. Despite titration of morphine and switching to other opioids, her pain remains uncontrolled, and she is yelling out in delirium. The patient’s condition is not amenable to any surgical or procedural intervention, and she has expressed that she knows “she is living on borrowed time.” The concept of a midazolam infusion is brought up to sedate the patient for her comfort. The patient and family agree with this approach and want to put comfort first, even if the patient is comatose.

Which one of the following is the next step?

a. Comply with the patient’s wishes and titrate the midazolam infusion to a level of comfort acceptable to her, even if this means she is unable to communicate

b. Refuse to comply with the patient’s wishes because palliative sedation can cause respiratory depression and inability to protect her airway

c. Comply with the patient’s wishes, but only to a level that allows her to communicate freely with her family

d. Comply with the patient’s wishes, but be certain to start intravenous dextrose/saline because she will be unable to eat and will otherwise die of dehydration/starvation

e. Refuse to comply with the patient’s wishes because this is physician-associated death, in that the midazolam may hasten her death

5. An 86-year-old woman with end-stage renal failure and end-stage chronic obstructive pulmonary disease is admitted to the intensive care unit with respiratory failure. A minimal dose of fentanyl (10 mcg/h with no boluses needed) is required to keep the patient sedated and comfortable while she receives mechanical ventilation. Her family thinks the patient would not want to live like this and requests removal of the ventilator and comfort measures to be implemented. All are in agreement with this decision and accept that the patient will die at the hospital. The number one goal of the family is to keep the patient comfortable. To this end, the physician wants to ensure that the patient will not experience any distress. An order for a 20-mg morphine bolus intravenously and midazolam bolus of 20 mg intravenous push is requested at the time of extubation.

Which one of the following is true regarding this request?

a. The request is reasonable and appropriate given the situation. This case illustrates the accepted medical practice of “withdrawing life-sustaining treatment.” The doctrine of double effect allows one to use medications that may hasten death if the goal is to promote comfort

b. The request is unreasonable because the dose of medications is inappropriate. This situation could be constituted as physician-assisted death, in that it violates the doctrine of double effect. The drugs introduce a new cause of death (overdose of medication), and the response is not proportionate to the needs of the patient

c. This request is reasonable because it results in the cause of death being undoubtedly the underlying respiratory and renal failure, not the medications. The doctrine of double effect allows one to use medications that may hasten death if the goal is to promote comfort

d. This request is reasonable because it promotes a dignified end for the patient, with no suffering

e. The request is unreasonable because the patient does not have an advance directive stating her wishes regarding withdrawal of mechanical ventilation in this setting