Palliative Sedation
Clinical and Ethical Perspectives

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Disclosure

- No relevant financial or commercial disclosures

Principlism

- Autonomy
- Beneficence
- Nonmaleficence
- Justice

Palliative Sedation

- The use of medications to intentionally induce decreased level of consciousness as a means to manage severe and refractory symptoms
- Usually, but not necessarily, maintained to the patient's death

Refractory/Intractable Symptoms

- A symptom is considered "refractory" or "intractable" when:
  - > adequate relief cannot be obtained
  - > relief cannot be obtained without intolerable side effects
  - > relief cannot be obtained within an acceptable timeframe
  - > patient reports intolerable suffering in regards to the symptom regardless of management

Symptom Frequency

Annals of Oncology 20: 1163–1169, 2009
doi:10.1093/annonc/mdp048

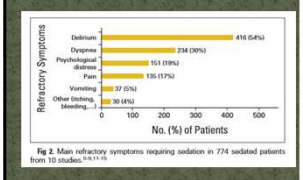


Fig 2. Main refractory symptoms requiring sedation in 774 sedated patients from 10 studies.[6,9,11–15]

Table 3. Refractory symptoms requiring PST

Variable	Cohort A (PST)	
	n	%
Refractory symptom		
Delirium and/or agitation	210	78.7
Dyspnea	52	19.5
Pain	30	11.2
Vomiting	12	4.5
Psychological and physical distress	50	18.7
Only psychological distress	16	6.0
Others	10	3.7
Number of refractory symptoms		
1	168	62.9
2	89	33.3
3	9	3.4
4	1	0.4

PST, palliative sedation therapy.

Proportional/Proportionate Sedation

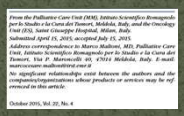

RESEARCH CMAJ

Considerations of physicians about the depth of palliative sedation at the end of life

CMAJ, April 17, 2012, 184(7)

- Multidimensional Notion
- Mild vs Deep
- "May aim for deep sedation from the start or choose for a more gradual approach. Proportionality refers not only to the titration of sedatives for the relief of refractory symptoms but also to titration to patients' preferences, communication needs, wishes of relatives and aesthetic consequences."

Proportional/Proportionate Sedation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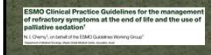
Palliative Sedation in Patients With Cancer
Marco Maltoni, MD, and Elisabetta Scarpi, MD

- Symptom-guided procedure, utilizing the minimum effect dose for sedation
- Requires monitoring to assess response to medication
- "Patients who are sedated can be talked to, wanted, cared for, and loved by their relatives, sometimes "answering" with their presence in surprising and unexpected ways"

Effect on Survival


ESMO Clinical Practice Guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation†


JOURNAL OF CLINICAL ONCOLOGY REVIEW ARTICLE
Palliative Sedation in End-of-Life Care and Survival: A Systematic Review

Impact of palliative sedation on patient survival

The limited data show that neither the administration of palliative sedation [48] nor the degree of sedation hastens death in otherwise terminally ill patients. These findings are illustrated in the following studies:

- The impact of sedation on survival for terminally ill patients was evaluated in a 2012 systematic review of observational studies involving over 1000 patients (34% of whom underwent sedation) [48]. There was no statistically significant difference in overall survival between hospice patients who underwent sedation (median, 7–27 days) and those who did not (median, 4–40 days) [48].
- Of three studies evaluating the degree of sedation and its impact on survival after withdrawal of ventilatory support, [49–51] the largest study evaluated 42 patients, of whom 88% were administered morphine during the procedure [49]. No association was reported between the dosages of morphine used and the duration of survival.

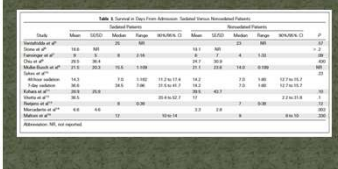


Table 3. Survival in Days From Admission: Sedated Versus Nonsedated Patients

Principle of Double Effect

- The doctrine of double effect was developed by the Roman Catholic church, dating back to the Salmanticenses theologians of the 16th and 17th centuries.
- It is applied to situations in which it is impossible to avoid all harmful actions, helping clinicians decide whether one potentially harmful action is preferable to another
- Example: Abortion

Principle of Double Effect

1. The nature of the act must be good or morally neutral and not in a category that is absolutely prohibited or intrinsically wrong.
2. The intent of the provider and procedure must be good. The bad effect can be foreseen, tolerated, and permitted.
3. A distinction between means and effects must be envisioned, in that death must not be the means to the good effect.
4. A proportionality between the good and bad effects must be substantiated by reason, in that the good effect must exceed or balance the bad effect.

Principle of Double Effect

Commentary:
Double Effect—Intention is the Solution, Not the Problem

Daniel P. Sulmasy

Journal of Law, Medicine & Ethics, 28 (2000): 26–29.

Responsibility vs. Culpability

one aims.[6] I have argued that one's *responsibility* covers the whole "package deal" of what one freely chooses to bring about, but that under certain circumstances such as those specified by the RDE, *culpability* (that for which one can be blamed) only covers what one intends.[7]

No serious proponent of the RDE says that someone who has hastened the death of a patient is not *responsible* for that outcome. The RDE only says that one is not *culpable* if one has followed its conditions and not violated any other moral rules. As Boyle once put it, "if there is no responsibility for side-effects, then it would hardly be relevant to state a moral condition for the permissibility of bringing them about."[8]

Principle of Double Effect


SOUNDING BOARD

The Rule of Double Effect — A Critique of Its Role in End-of-Life Decision Making

NEJM 1997;337:1768-1771

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- For clinicians and others who believe in an absolute prohibition against actions that intentionally cause death, the rule of double effect may be useful as a way of justifying adequate pain relief and other palliative measures for dying patients. But the rule is not a necessary means to that important end.
- The rule's absolute prohibitions, unrealistic characterization of physicians' intentions, and failure to account for patients' wishes [autonomy] make it problematic in many circumstances.

Euthanasia

- The use of medications to intentionally induce death as a means to manage severe and refractory symptoms
- Example: Netherlands
- (2002) Termination of Life on Request and Assisted Suicide (Review Procedures) Act
- Pancuronium – Stop breathing
  - No sedating or analgesic effects

Pitfalls for Injudicious Use

- Inadequate patient assessment in which potentially reversible causes of distress are missed
- Failure to engage expert clinicians in relief of symptoms
- The case of an overwhelmed physician resorting to sedation because he is fatigued and frustrated by the care of a complex symptomatic patient
- Demand for sedation is generated by the patient's family/proxy and not the patient him/herself

Society Position Statements

Palliative sedation is ethically defensible when used 1) after careful interdisciplinary evaluation and treatment of the patient, and 2) when palliative treatments that are not intended to affect consciousness have failed or, in the judgment of the clinician, are very likely to fail, 3) where its use is not expected to shorten the patient's time to death, and 4) only for the actual or expected duration of symptoms. Palliative sedation should not be considered irreversible in all circumstances. It may be appropriate, in some clinical situations when symptoms are deemed temporary, to decrease sedation after a predetermined time to assess efficacy, continued symptoms and need for ongoing sedation.

Position Statement

The Hospice and Palliative Nurses Association:

- Affirms the value of palliative care, including hospice care that includes aggressive and comprehensive symptom management.
- Affirms the use of palliative sedation in imminently dying patients to manage refractory symptoms unrelieved by optimal palliative care.
- Asserts that hospice and palliative nurses must understand palliative sedation, and its ethical and legal justifications for use.

Society Position Statements

Code of Medical Ethics Opinion 5.6

The duty to relieve pain and suffering is central to the physician's role as healer and is an obligation physicians have to their patients. When a terminally ill patient experiences severe pain or other distressing clinical symptoms that do not respond to aggressive, symptom-specific palliation it can be appropriate to offer sedation to unconsciousness as an intervention of last resort.

Palliative sedation is an important tool among the spectrum of therapies available in hospice and palliative care. For the small number of imminently dying patients whose suffering is intolerable and *refractory*, NHPCO supports making the option of palliative sedation, delivered by highly trained health care professionals, available to patients.

Psychological distress and existential suffering

- "Psychological distress and existential suffering are complex and challenging. These terms encompass issues such as meaninglessness of life, sense of hopelessness, perception of self as a burden to others, feeling dependent on others, feeling isolated, grieving, loss of dignity and purpose, fear of death of self, or fear of the unknown"

Maltoni M, Setola E: Palliative Sedation in Patients With Cancer. Cancer Control (2015). 22(4): 436.

Psychological distress and existential suffering

Although the Academy recognizes that existential distress may cause patients to experience suffering of significant magnitude, there is no consensus around the ability to define, assess, and gauge existential suffering, to measure the efficacy of treatments for existential distress, and whether it is in the realm of medicine to palliate such suffering when it occurs absent of physical symptoms. Patients with existential suffering should be thoroughly assessed and treated through vigorous multidisciplinary efforts which may include involving professionals who are not usual members of the palliative care team (e.g., experts in psychological, family therapy, or specific spiritual services). If palliative sedation is used for truly refractory existential suffering, as for its use for physical symptoms, it should not shorten survival.

Physicians may offer palliative sedation to unconsciousness to address refractory clinical symptoms, not to respond to existential suffering arising from such issues as death anxiety, isolation, or loss of control. Existential suffering should be addressed through appropriate social, psychological or spiritual support.

Medications commonly used for PS

- Benzodiazepines
  - Midazolam
  - Lorazepam
- Neuroleptics
  - Haloperidol
  - Chlorpromazine
- Barbiturates
  - Phenobarbital
- Propofol

Benzodiazepines

- Midazolam
  - Pharmacology
    - Water soluble, short-acting
    - Metabolized to lipophilic compound that rapidly penetrates CNS
  - Loading dose: 1mg to 5mg
  - Starting dose: IV or SQ infusion at 0.5mg/hr to 1mg/hr
  - Maintenance dose
    - 1mg/hr to 20mg/hr (can intermittently administer 1mg to 5mg during infusion as needed)
  - Advantages: Rapid onset
  - Side effects: paradoxical agitation, respiratory depression, hiccups, n/v

Benzodiazepines

- Lorazepam
  - Pharmacology
    - Elimination not altered by renal/hepatic dysfunction
    - Peak effect approx. 30mins after IV administration
    - Slower pharmacokinetics ∴ less amenable to rapid titration
  - Starting dose:
    - IV or SQ at 0.5mg/hr to 1mg/hr
    - SL at 1mg to 5mg every 1hr to 4hr (unpredictable absorption)
  - Maintenance dose
    - IV or SQ at 4mg/day to 40mg/day (titrate by 1mg Q2H)
  - Advantages: Rapid onset
  - Side effects: paradoxical agitation, hypotension, abdominal discomfort, nausea

Neuroleptics

- Haloperidol
  - Pharmacology
    - Non-selectively blocks postsynaptic D_2 receptors
  - Starting dose:
    - IV or SQ or PO at 0.5mg to 5mg Q2-4hours or
    - For continuous infusion (SQ or IV):
      - 1mg to 5mg bolus then 0.5mg/hr to 1mg/hr
  - Maintenance dose:
    - 5mg to 15mg per day (increase infusion rate by 0.5mg/hr)
  - Side effects: EPS, NMS

Neuroleptics

- Chlorpromazine
  - Pharmacology
    - Blocks postsynaptic D_2 receptors
    - Strong alpha-adrenergic blocking effect
  - Starting dose:
    - IV at 12.5mg Q4-12H
    - PR at 25mg to 100mg Q4-12H
  - Maintenance dose:
    - IV infusion at 3mg/hr to 5mg/hr
    - PR at 75mg to 300mg per day
  - Side effects:
    - Orthostatic hypotension, EPS, paradoxical agitation, anticholinergic effects

Barbiturates

- Phenobarbital
  - Pharmacology:
    - Depresses sensory cortex, decreases motor activity, alters cerebellar function to produce drowsiness and sedation
  - Starting dose:
    - IV or SQ bolus at 1mg/kg to 3mg/kg followed by starting infusion at 0.5mg/kg/hr
    - PO or PR bolus is 200mg
  - Maintenance dose: 50mg/hr to 100mg/hr
    - IV or SQ increase in 1mg/kg/hr increment to maintain sedation
    - PO or PR increase in increments of 30mg
  - Advantages: Rapid onset
  - Adverse effects:
    - paradoxical excitement in elderly, hypotension, Stevens-Johnson syndrome, angioedema, rash

Propofol

- Pharmacology:
  - Short-acting lipophilic IV general anesthetic
- Starting dose: 0.5mg/kg/hr
- Maintenance dose: 1-4mg/kg/hr
- Advantages:
  - Rapidly causes unconsciousness
  - Easy to titrate
- Adverse effects:
  - Hypotension, involuntary body movements, apnea